INDEX NUMBER

Vol. 21 JUNE, 1947 No. 6

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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FROM AN ORIGINAL ETCHING BY ERNEST D. ROTH

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Advances in the exacting science of surgery are continually being made through broad and carefully integrated programs of research. A similar program of research is being carried out by Davis & Geck, Inc. to promote advances in surgical sutures. The results are evident in the improving quality and increasing variety of D & G products available to the surgical profession.

SUTUREGRAM

NUMBER TWO IN A SERIES

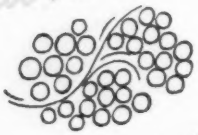
Sutured Strength: Sutured strength of a wound is determined by:

1. Knot strength of sutures used
2. Capacity of tissues to hold sutures
3. Number of sutures used

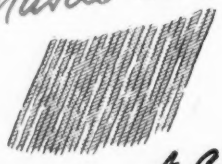
For example if thread strength ⟷ of a suture is 10 lbs., then knot strength ○ is 5 lbs.

However, one suture pulls out of...

Fat at 1/4 lb.



Muscle at 1/4 lb.



Skin at 9 lbs.

Fascia at 8 lbs.

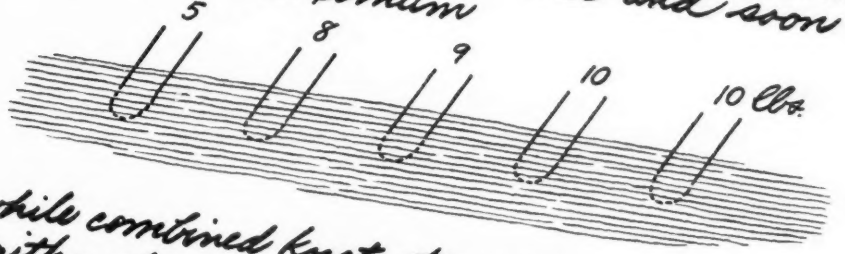
This capacity to hold sutures is increased in the following manner by adding sutures

Fat.....	two sutures	1/4 lb. ...	three 1/4 lb.
Fascia.....	" "	10 lbs. ...	" 11 lbs.
Muscle....	" "	3/8 lb. ...	" 1/2 lb.
Skin.....	"	10 lbs....	" 12 lbs.

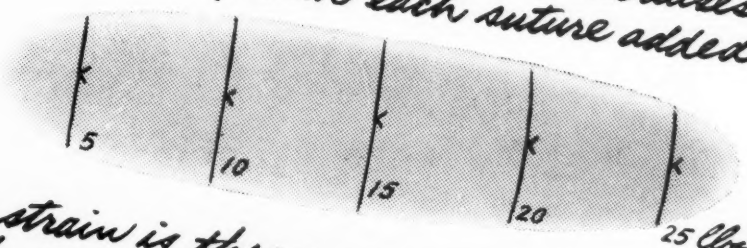
SUTUREGRAM NUMBER TWO (CONTINUED)

In other words, sutured strength is increased most by adding sutures to fascia. Very fine sizes can be used in all other tissues because they have no capacity to hold sutures.

Conversely because capacity of tissues to hold sutures increases only by an increment as each new suture is added and soon reaches a maximum



while combined knot strength increases arithmetically with each suture added,



less strain is thrown on each suture as each new one is added to a wound.

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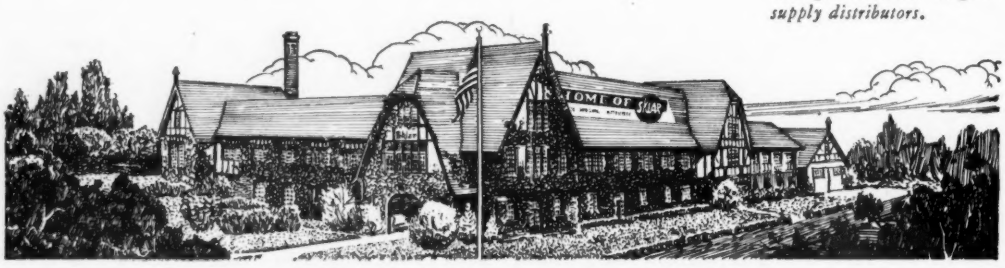

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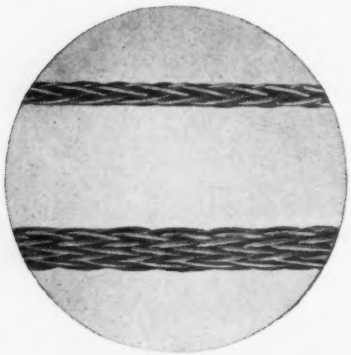

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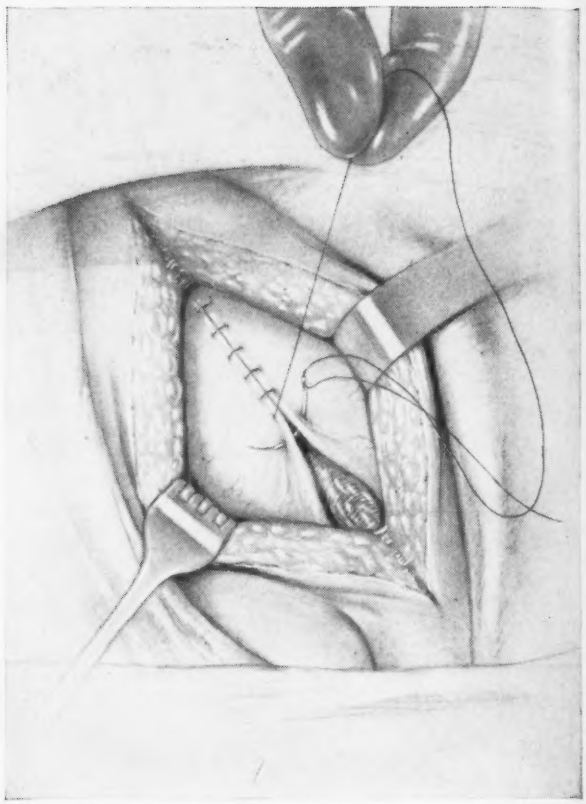

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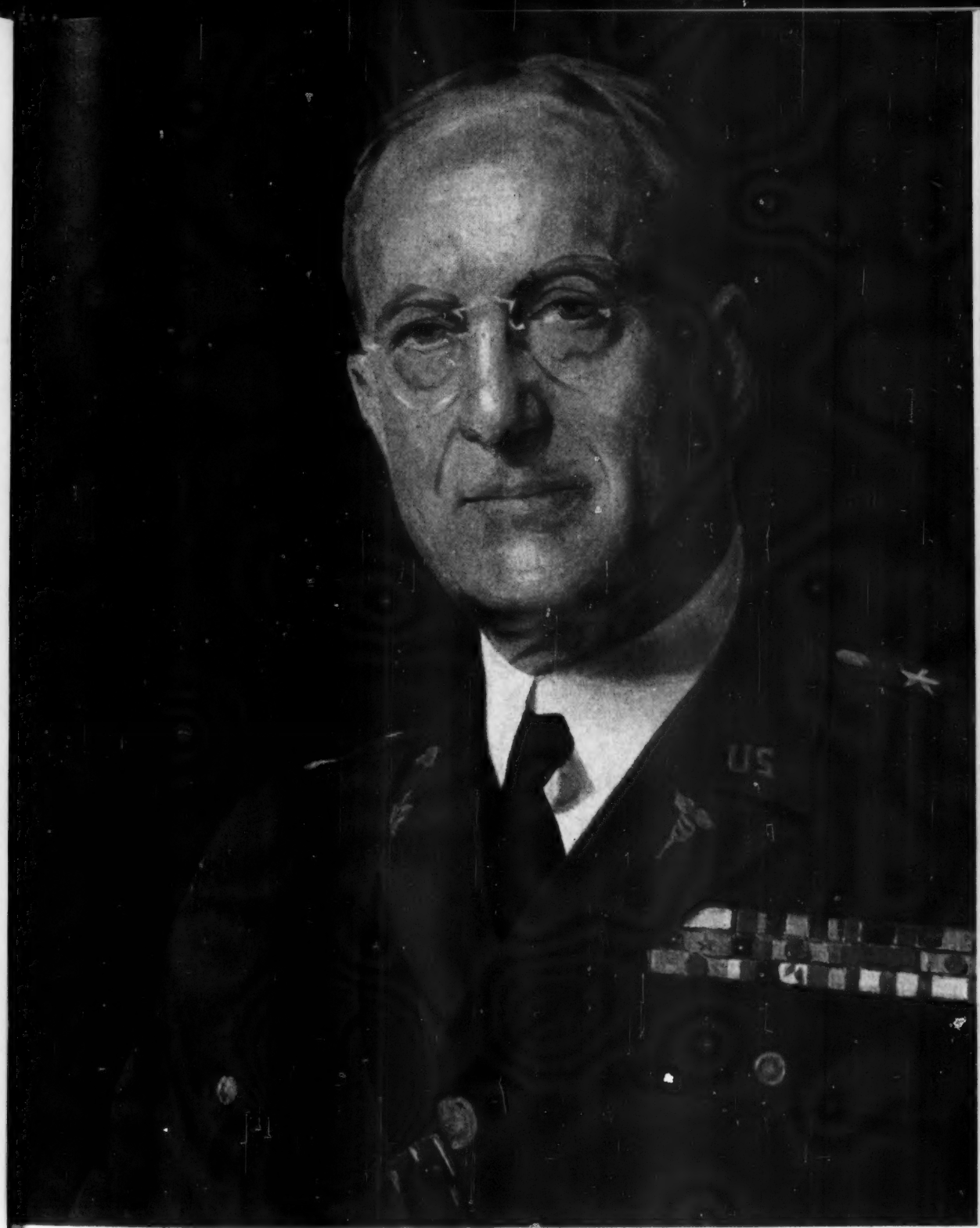

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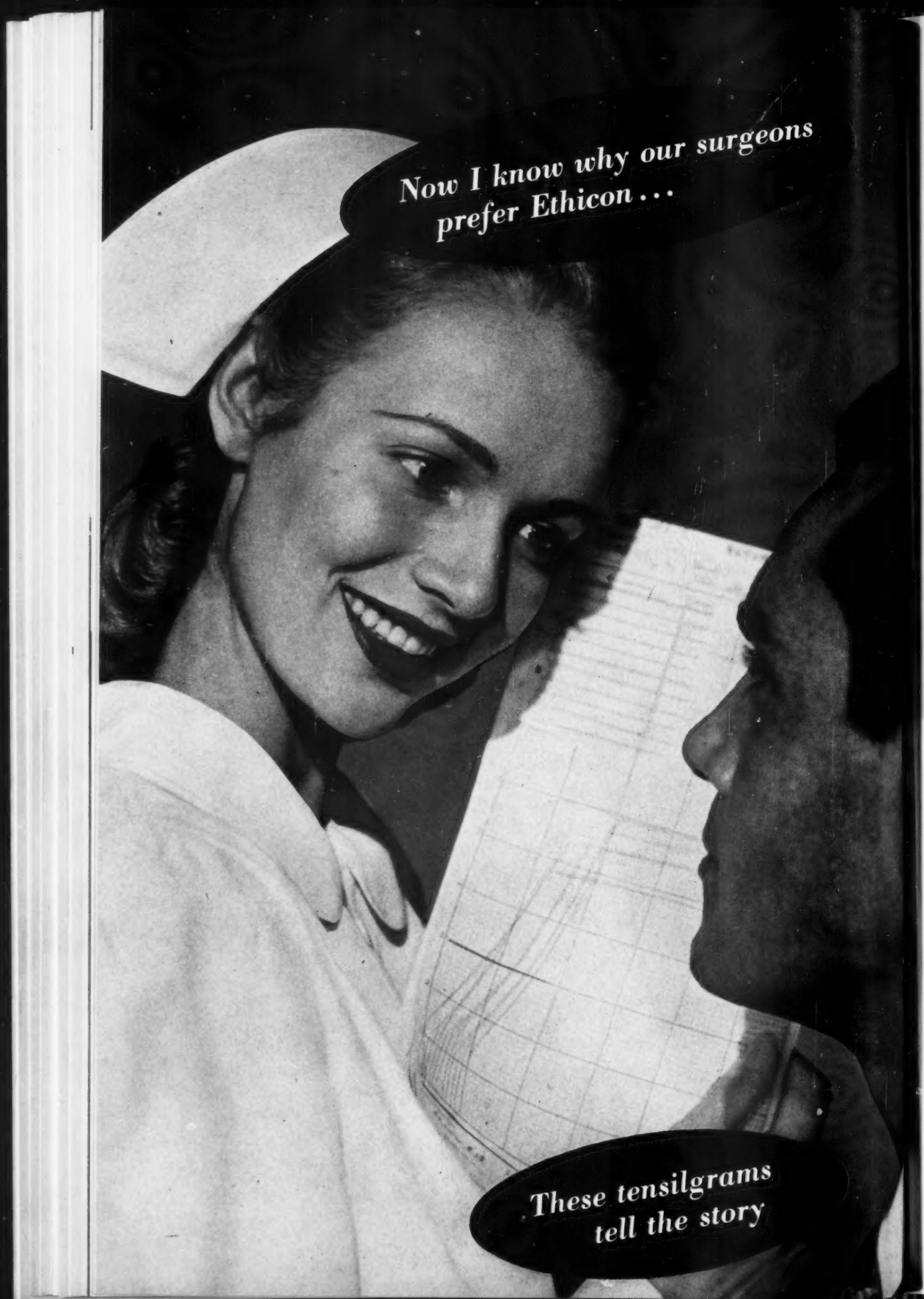
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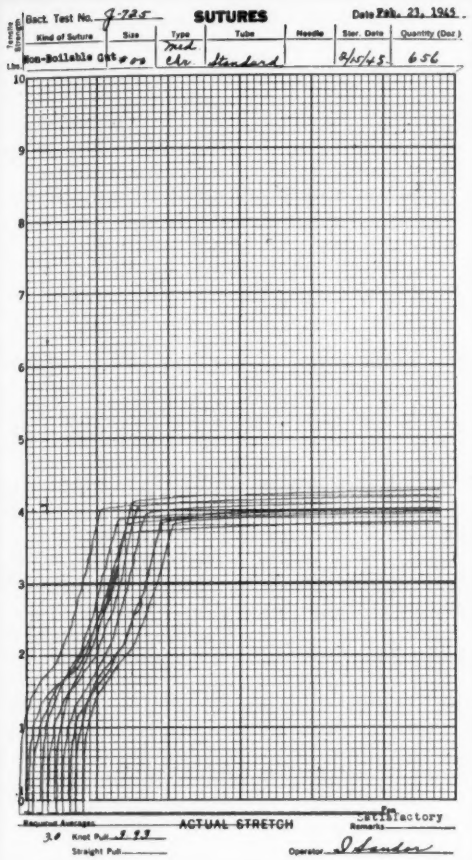

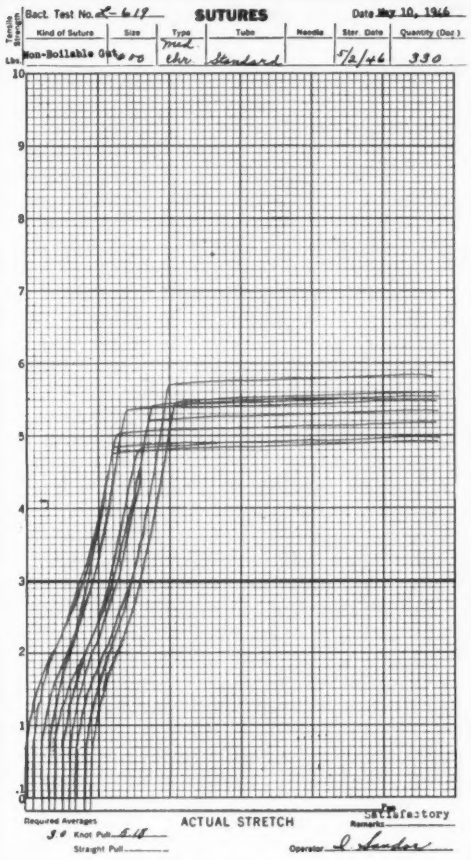

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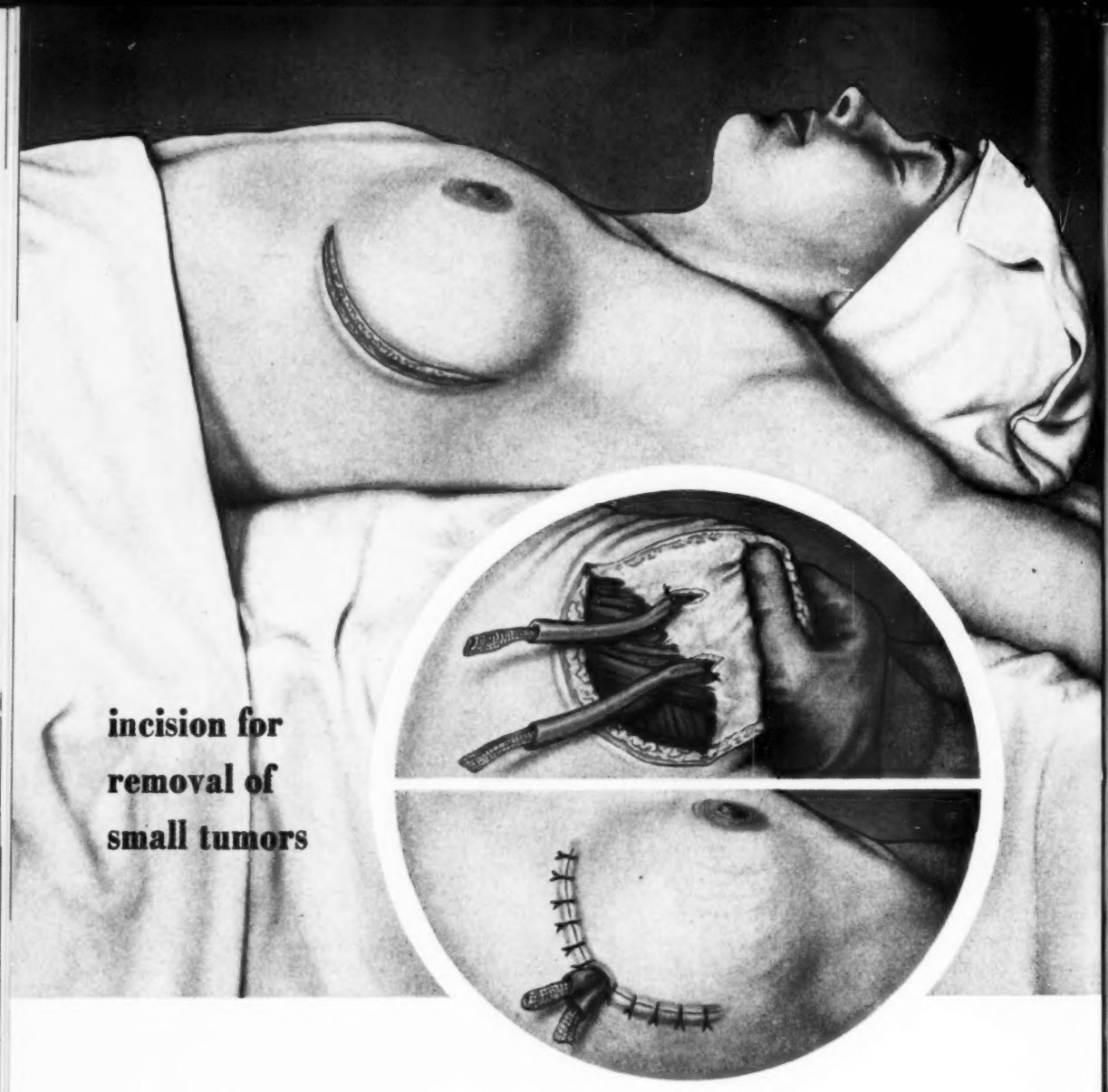

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THE SURGICAL TREATMENT OF HYPERTENSION

III. THE "NEUROGENIC" VERSUS RENAL HYPERTENSION FROM THE STANDPOINT OF OPERABILITY

GEZA DE TAKATS, M.D., AND EDSON FAIRBROTHER FOWLER, M.D., CHICAGO, ILL.
(From the Department of Surgery, University of Illinois College of Medicine, and St. Luke's Hospital)

INTRODUCTION

ALL classifications of hypertension contain a differentiation between a nonrenal and a renal type of hypertension. It is generally assumed that the so-called neurogenic type of hypertension is the ideal case for splanchnic nerve section. In fact, an effort has been made to differentiate the neurogenic from the renal hypertension by the response of the patient's blood pressure to high spinal anesthesia.[1] In addition, Grimson proposed total sympathectomy in man, because in his experimental neurogenic hypertension, produced by section of the buffer nerves, more limited procedures such as splanchnic nerve section and dorsolumbar sympathectomy were of little avail.[2]

Our experience, however, has not supported the view that the nonrenal hypertensives do better after operation than the lesions with definable renal lesions. In our series of fifty cases recently reported elsewhere,[3] an attempt has been made to define these groups so that a comparison of results can be made between them (Table I). Naturally the extent of vascular damage, as developed by our grading, has a potent influence within the groups.

THE "NEURO-ENDOCRINE" GROUP

Experimentally a number of methods are known to produce acute or chronic neurogenic hypertension; they have been concisely summarized in the monograph of White and Smithwick.[4] Page[5] gave a classic description of a "diencephalic" syndrome in man, consisting of flushing of the face and neck, excessive perspiration, tachycardia, and hyperperistalsis, much like the cat exhibits when its midbrain is stimulated. However, such cases readily merge with the endocrine group, notably the ones seen at the menopause. For this reason, for lack of concise endocrine assays, we have pooled the whole group of patients in whom a primary renal hypertension could be excluded.

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TABLE I. CLASSIFICATION OF PATIENTS SUFFERING FROM "ESSENTIAL" HYPERTENSION (FIFTY PATIENTS OPERATED UPON)

NONRENAL	NUMBER OF CASES	RENAL	NUMBER OF CASES
"Neurogenic"	3	Unilateral renal disease	4
Endocrine	2	Renal trauma	2
Atheromatous	3	Toxemia of pregnancy	6
		Pyelonephritis	3
		Scarlet nephritis	5
		"Rheumatic kidney"	3
Total	8		23
Unclassified	19		

It would seem reasonable to predict the postoperative results by blocking the extent of sympathetic outflow which one intends to remove surgically. Both spinal anesthesia[1] and paravertebral sympathetic block[6] have been suggested for this purpose. In the surgery of the sympathetics controlling the extremities this has certainly been the practice of our group.[7] However, our experience with these methods in hypertensives has not been satisfying. Elderly persons with arteriosclerosis with high pulse pressures due to a rigid, nondistensible aorta are notorious for the hypotensive effects of spinal anesthesia (Fig. 1). Splanchnic block by the posterior route, the dangers of which one of us has previously described,[8] may produce marked fall in blood pressure due more to the toxic reaction to procaine or to a vasovagal reflex than to the effect of blocking the vasoconstrictor fibers. And finally there seems to be a type of nonrenal hypertension in which diffuse arteriolar resistance is maintained in spite of blocking the sympathetics of the area (Case 4). Vasopressin of the posterior lobe of the pituitary, which is under nervous control, may be one such mechanism.*

Germane to this discussion are the experimental findings of Walter and Pijoan[9] who, while trying to produce diabetes insipidus observed a persistent hypertension in a dog whose third ventricle was punctured in the midline. This dog had a pressure of 242/130 and gradually developed tortuous arteries and nicking of the veins in the retina. A 23 per cent cardiac enlargement took place in four months. Nembutal depressed the pressure to 120/60; the cold pressor reaction was exaggerated. Insulin hypoglycemia was followed by a marked pressor response. In contrast to this a dog on which the Goldblatt clamp had been used showed a fixed hypertension with not much variation in pressure after pressor or depressor stimuli.

To satisfy our criteria of nonrenal hypertension, the following findings were postulated.

1. Normal renal structure in a hypertension of long standing. Such cases have been reported before. Striking is the case of Shapiro[10] who found no evidence of any renal impairment at the autopsy of a woman who suffered from a hypertension of more than twenty-five years' duration. In our material, normal biopsies were reported in six out of thirty-five cases, an incidence of 17 per cent. In the series of Castleman and Smithwick[11] 7 out of 100 patients

*Rydin, H., and Verney, E. B. (Quart. J. Exper. Physiol. 27: 343, 1938) showed that inhibition of water diuresis can be obtained after emotional stress or muscular exercise, when the kidneys and adrenals are denervated and both splanchnic nerves cut.

were graded as having normal kidneys, and 21 per cent as having grade 1 (mild) involvement (Case 1).

2. History of a previous thyroidectomy for a toxic goiter, which occurred in six of our fifty-two patients. When blood pressures were available at the time of thyroidectomy, they were reported as being high; in fact, some thyroidectomies were undertaken to reduce blood pressure. Such thyroid stimulation presumably on a pituitary basis is suggestive of a pituitary type of hypertension, which Griffith and his associates have especially promulgated.[12] We present three cases of this type (Cases 2, 3, and 4).

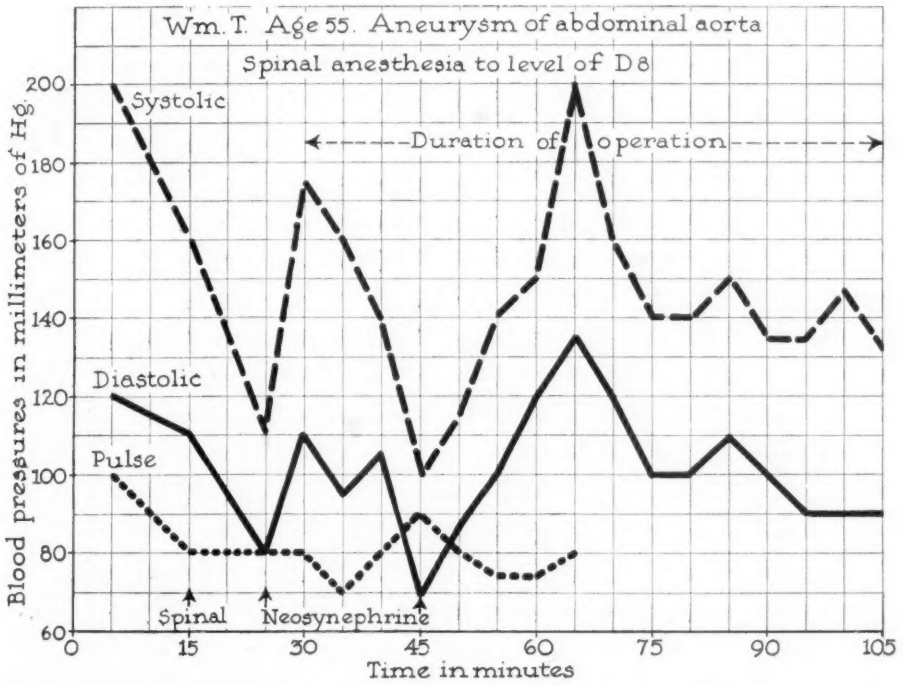

Fig. 1.—Hypotensive effect of spinal anesthesia on a patient suffering from arteriosclerosis of the aorta. This patient's blood pressure fell from 200/120 to 110/80 mm. of mercury in twenty-five minutes. While the pressure was elevated with neosynephrine temporarily, at the forty-fifth minute the pressure fell again to 100/70 mm. of mercury. Certainly this patient had anything but neurogenic hypertension; he had severe arteriosclerosis leading to a huge aneurysm of the abdominal aorta. The operation was not started until the first dip in pressure occurred, so that neither bleeding nor nervous stimuli from the field of operation could have been responsible for the hypotension.

3. Finding of a medullary or cortical tumor of the adrenal, which is not within the scope of this paper, can be best investigated by the combination of an intravenous pyelogram with air insufflation around the kidney (Fig. 2) and the recently developed histamine response of such patients.[13]

CASE REPORTS

CASE 1.—M. Z., 21-year-old unmarried woman, entered St. Luke's Hospital on June 15, 1941. With the exception of intermittent headaches, there were no complaints. One of these headaches was very severe, lasted a whole day, and was accompanied by nausea and vomiting. She had fallen from a horse several times; this was followed by dizziness for a day. There was some nycturia at times. She was rather high-strung, temperamental, readily upset.

Entrance.—The patient's blood pressure was 160/100. Physical examination was negative. Eye grounds were normal. The heart occupied 40 per cent of the thorax. The electrocardiogram was normal. The urine was negative for pathologic elements. The intravenous pyelogram suggested a small and deformed left renal pelvis, but the retrograde pyelogram did not bear this out. Phenolsulfonphthalein excretion was 35 per cent in one hour; the urea clearance was 58 per cent (standard). Blood chemistry was normal. Sodium amytal

Fig. 2.—Around the left kidney 200 c.c. of air have been injected in a 20-year-old girl with hypertension and hirsutism, in whom a cortical adrenal tumor was suspected. This view was taken twenty-four hours later and shows a perfectly normal triangular shadow above the upper pole of the left kidney, separated from it by an envelope of air.

depressed the blood pressure from 170/104 to 135/80 mm. of mercury. The cold pressor test raised it from 160/100 to 190/120.

Operations.—Operations were done on June 26 and July 9, 1941, at which time right and left splanchnic nerve sections were done together with a dorsolumbar sympathectomy. Both chains were cut between the ninth dorsal and second lumbar ganglia. The kidneys, ureters, and adrenals were normal. A biopsy taken from the right kidney revealed no pathologic changes.

Course.—The patient was discharged with blood pressures of 140/80, 120/80, and 80/0 in the three positions. The cold pressor response was minimal after the operation (140/80 to 145/80). She continued to have occasional headaches but lived a healthy outdoor life, taking on the job of a wrangler on one of the western ranches. The blood pressures fluctuated between 160-130 systolic and 100-80 diastolic during the next three years. Postural hypotension had disappeared. In May, 1944, she had a spell of unconsciousness with a blood pressure of 90/60 mm. of mercury, from which she temporarily recovered, but died suddenly in a second attack on May 28, 1944, not quite three years after operation. At autopsy no anatomic cause for death was found. The kidneys both grossly and microscopically were normal. Nothing was found in the brain.

Comment.—This was a case of a nonrenal hypertension, for which no cause could be found at autopsy. Note that a complete splanchnic section did not materially influence the blood pressure for the follow-up period of three years. This observation will be later discussed on the basis of other "neurogenic" cases.

CASE 2.—R. K., a 24-year-old white man, was admitted to the Research and Educational Hospitals on Jan. 25, 1941, complaining of nervousness and tremor.

Past History.—He had been nervous and jittery ever since he could remember. Two and one-half years before, at the age of 22 years, he had an eye infection, at which time a systolic blood pressure of 140 mm. of mercury was discovered. He was referred then to the University Dispensary where a blood pressure of 170/110 and a basal metabolic rate of +27 per cent were discovered. No treatment was described and the blood pressure dropped to 132/76. One year before admission a blood pressure of 210/120 was obtained which fell on bed rest to 135/80. Other past history was not contributory.

Entrance.—The patient's blood pressure was 150/90 mm. of mercury. The fundi were negative. The heart and electrocardiogram were normal. Urine analysis was negative. He could concentrate urine to 1.031; 40 per cent of the dye was eliminated in fifteen minutes. The urea clearance was 40.12 c.c. The intravenous pyelogram was normal. The basal metabolic rate was +7 per cent. Under sodium amytal the blood pressure dropped to a minimum of 120/65.

Operations.—Operations were done on March 18, 1941, and April 1, 1941. Convalescence was uneventful except for a transitory left hydropneumothorax. When the patient left the hospital the blood pressure was 120/74 lying down, 120/70 sitting, and 95/55 in the standing position. No renal biopsy is available.

Course.—Six weeks after discharge the blood pressure was 118/78 sitting and 106/78 in the standing position. He felt better but had not yet returned to work. Two and one-half years later the blood pressure was 133/92, 130/90, and 142/94 in the three positions. He had no symptoms and worked a full day.

Comment.—Based on the early juvenile type of markedly fluctuating blood pressure, on the prominence of nervousness, tremor, and a single elevated metabolic rate, which was found normal at a later date, the diagnosis of a "neurogenic" or perhaps pituitary type of hypertension might be hazarded. The indifferent response to splanchnic section is a further indication in our minds that the mechanism of the hypertension may not be mediated by the splanchnic nerves.

CASE 3.—D. T., a 46-year-old housewife, entered St. Luke's Hospital on Jan. 22, 1942, complaining of dyspnea on exertion, palpitation, nervousness, cold extremities for five years, and severe occipital headaches for six months.

Past History.—The patient had had scarlet fever at the age of 5 years. She had six pregnancies with two abortions. An elevated blood pressure was noticed after the fourth pregnancy in 1933. A thyroidectomy was done in 1936. Menopausal symptoms have been noted in the past two years. Blood pressure was 160/90 in 1933, 176/96 in 1934. In the past two years she had received theelin, which reduced the blood pressure slightly.

Entrance.—At time of admission, pressure was 192/104. Eye grounds revealed moderate angiospasm, tortuosity, and nicking of the veins. A soft systolic murmur was heard at the apex. The heart occupied 49 per cent of the thorax; electrocardiogram revealed minimal changes. The basal metabolic rate was –4 per cent. The intravenous pyelogram showed a freely movable right kidney with slight hydronephrosis and somewhat delayed function; left kidney seemed normal. The phenolsulfonphthalein excretion was 35 per cent in fifteen minutes. Concentration-dilution tests ranged between a specific gravity of 1.025 to 1.004 of the urine. The urea clearance was 69.0 standard. Blood chemistry was within normal limits. Cholesterol was 260 mg. per 100 c.c. of blood. Sodium amytal depressed the pressure from 178/96 to 108/70. The cold pressor test raised it from 186/90 to 190/100. Epinephrine raised it from 160/85 to 175/85. On bed rest the pressures varied between 210/98 and 130/76. She was quite emotional and had hot flashes.

Operations.—Operations were performed on Feb. 2, 1942, and March 6, 1942. She was discharged on March 17 with blood pressure of 156/86, 142/84, and 68/32 in the three positions. Renal biopsy showed focal, hyaline fibrous thickenings of the glomerular tufts and moderately thickened muscular walls of the arteries.

Course.—Four months after operation the blood pressure was 200/110 in the horizontal and 150/100 in the vertical position. She was just as anxious and unstable as ever. On examination for the extent of the denervated area, lack of sweating was complete from the ninth dorsal to the first lumbar on the left and from the tenth dorsal to the second lumbar on the right side. She was placed on small doses of stilbestrol which she had been taking before. She was heard from twenty months postoperatively when the blood pressure was 182/102 lying down, 174/104 sitting, and 170/100 standing. She did a full day's work, but flushes and dizziness were present.

Comment.—This patient's blood pressure had fluctuated markedly for many years. She had a thyroidectomy for "nervousness" and tachycardia. She responded only very slightly to epinephrine and to cold as if the vasospasm had been continuous. On one occasion, when a sham injection of saline solution was given preoperatively, her blood pressure was 150/85 when she stated that her blood pressure was going up, her face was warm, and that she knew her pressure was very high. When nurses took the pressure, it was always 20 to 30 points lower. It was felt preoperatively that a severe psychoneurosis was present, but treatment directed toward this factor did not lower the blood pressure.

Technically the operation was complete; the immediate postural hypotension was marked and the area of denervation was satisfactory. One is forced to conclude that the mechanism increasing peripheral resistance was not mediated through the splanchnics. The renal damage was slight and patients with much more severe damage responded well. While we have no hormonal assays one is forced to suspect the pituitary mechanism, either through the antidiuretic or the adrenotropic principle.[12(b)] Pituitary irradiation was suggested but not carried out. Adequate simple clinical tests for this type of hypertension are still lacking.

CASE 4.—F. F., a 39-year-old telephone test man, was admitted to St. Luke's Hospital on Jan. 27, 1942. The hypertension had been discovered only two months previously during a routine physical examination. The only symptom consisted of occipital headaches on rising.

Past History.—Past history was noncontributory. The dull occipital headache started around Christmas, 1941. He did not respond to adequate doses of potassium thiocyanate.

Entrance.—The patient's blood pressure was 220/130. Physical examination was essentially negative. Eye grounds revealed marked angiospasm with occasional pin-point hemorrhages and scattered small exudates (grade 3 retinopathy). Heart was normal in size. Electrocardiogram revealed no significant changes. The intravenous pyelogram revealed a large right and a smaller left kidney with some hydronephrosis on the right. Both pelves were intrarenal. However, the retrograde pyelogram revealed no obvious pathologic changes; the dye appeared at the left ureter in less concentration than on the right. The urine contained no pathologic elements. Concentration-dilution test varied between 1.013 and 1.004. The urea clearance was 48, standard. Sugar tolerance was normal and roentgenograms of the sella turcica revealed no pathologic changes. Blood chemistry was within normal limits. Sodium amytal depressed the blood pressure 185/112 to 166/116; intravenous sodium pentothal from 195/130 to 180/115. Epinephrine given intravenously changed the pressure from 174/108 to 210/90; the cold pressor response raised it from 178/114 to 188/122.

Operations.—On March 11, 1942, a right-sided splanchnic nerve section and dorsal sympathectomy from the ninth to twelfth dorsal were done. There was continuous oozing throughout the operation and patient's condition was so unsatisfactory that the section of the lumbar chain was postponed. Eight days later the right lumbar chain was sectioned below the third lumbar and above the first lumbar, the previous stump of the chain being recognized. The right kidney seemed normal in size, color, and consistency. A small biopsy was taken which revealed normal glomerular tufts and the usual convoluted tubules. Occasional slight hyaline thickening and moderately cellular tubular linings were observed. The blood vessels seemed normal. The biopsy was graded as 0–1. On March 28, 1942, the left splanchnic nerves were excised, together with the chain f e ninth to the twelfth dorsal. Again the patient's pressure fell to low levels under the anesthetic; there was much capillary oozing. The kidney and adrenals, as on the right, seemed normal. The dorsal sympathetic chain seemed unusually large in comparison with the slender splanchnic nerve.

Course.—On discharge, the blood pressure was 172-115, 170/120, and 146/110 in the three positions. The patient was free from headaches for a while. One and one-half years after operation the blood pressure was 170/120. He was working full time. Following this he was placed again on potassium thiocyanate, to which he responded, while being resistant to the drug before the operation. Two and one-half years after operation he is working full time, and while on the drug the blood pressure stays around 160/105.

Comment.—The noteworthy facts about this case are: resistance to thiocyanate, resistance to heavy doses of barbiturates in the preoperative tests, poor response to the cold pressor test, marked fall in blood pressure and venocapillary oozing under general anesthesia, in spite of advanced retinal changes, a practically normal renal biopsy, and failure of the operations to lower blood pressure in any position. It might be objected that the lack of postural hypotension is due to the nonremoval of the left lumbar chain; however, with the total excision of both splanchnics and the removal of the right chain from the ninth dorsal to the third lumbar, some hypotension is observed at least immediately after the operation.

One is forced to conclude that this hypertension is nonrenal in origin and not one that is mediated to any extent through the splanchnic nerves. If it is diencephalic, it may still be activated through the pituitary gland. Hormonal studies in such cases are sorely needed.

THE RENAL GROUP

It should be made clear that we are not discussing patients suffering from clinically obvious glomerulonephritis or pyelonephritis. The patients whom we have grouped under this heading are those who are customarily classified as having essential hypertension, that is, there are no, or minimal, urinary findings and the renal functional impairment is commensurate with the duration of a chronic, slowly progressive hypertension. But the history correlated with the renal biopsies allows us to recognize individual characteristics in these groups.

Unilateral Hypoplastic Kidney.—It is well known that removal of small hypoplastic kidneys of congenital origin, or those which have atrophied because of a chronic unilateral pyelonephritis, may relieve hypertension. Goldring and Clasis[14] have collected seventy-six published cases in which unilateral nephrectomy was done for high blood pressure. Of these, only seven patients (9 per cent) had a return of blood pressure to normal for a period of two to five years. Personal experience with two children and one adult who were seen in the malignant phase of the disease indicated to us the great importance of recognizing the congenital hypoplastic kidneys early by taking blood pressure readings routinely in children. In previous publications[15] we have reported such cases. We wish to present, however, the type of case which is far more apt to be encountered and in which nephrectomy proved to be unsuccessful and splanchnic section beneficial.

CASE REPORTS

Case 5.—M. H., a 34-year-old housewife, was admitted to St. Luke's Hospital on May 4, 1942, complaining of nervousness, fatigue, dizzy spells, and headaches of ten months' duration.

Past History.—There was a negative family history and no past illnesses of significance. Ten months before, while at work, the patient had a sudden attack of fullness in the head, dizziness, and desire to shriek. This spell subsided and blood pressures of 220 to 180 systolic were observed. She was treated with high doses of vitamin A, theelin, and sedatives. She had two uncomplicated pregnancies. Seven years previously, while at a hospital for the removal of a benign tumor of the breast, a normal blood pressure was observed.

Entrance.—Blood pressure was 200/120. Eye grounds revealed some angiospasm. The heart occupied 42 per cent of the thorax. Electrocardiogram showed myocardial pathology. Basal metabolic rate was −3 per cent. The intravenous pyelogram revealed a normal left kidney as to size, shape, and position. The right kidney, however, was small and indistinct, giving the impression of agenesis. The retrograde pyelogram confirmed the diagnosis of a small, hypoplastic kidney. The dye appeared at 3 minutes from each ureter, in excellent concentration. The urologic consultant advised right nephrectomy.

The urea clearance was 40.7 (standard). Concentration-dilution varied between 1.020 and 1.004. The dye was excreted in fifteen minutes, up to 25 per cent. Sodium amytal depressed the blood pressure from 210/124 to 150/100; immersion into ice water raised it from 210/125 to 250/140; epinephrine 1:100,000 raised it from 200/125 to 260/130 and produced the symptoms she complained of.

Operations.—On May 11, 1942, the right kidney was explored. It was small, firm, and nodular, and had a coarsely scarred reddish surface. Since the other kidney was hypertrophic and well functioning a nephrectomy was done. No attempt was made to do a complete splanchnic section at this time, but the major splanchnic nerve was clipped and cut for later identification below the diaphragm. Convalescence was complicated by pneu-

mothorax on the same side and atelectasis on the other side. Histologic examination of the right kidney revealed a double pelvis with smooth linings. There was marked nephrosclerosis with local scars.

Course.—She was discharged with a pressure of 165/100 in the horizontal position and was re-admitted on Sept. 26, 1942. She felt well after the nephrectomy, but the blood pressure rose again to 194/110. The heart was enlarging. Blood chemistry was normal. On July 29, 1942, the left splanchnic nerve was cut from the seventh dorsal segment to the celiac ganglion and the dorsolumbar chain was excised between the tenth dorsal to below the first lumbar. She left the hospital with a blood pressure of 128/90, 120/110, and 98/88 in the three positions. Sixteen months later the blood pressure was 185/130, 170/124, and 160/120 in the three positions. She had no headaches, palpitation, or dizziness and worked eight hours daily at manual labor. Since the right splanchnic nerve was never excised, she was urged to have this operation, but was unwilling to do so because of lack of symptoms and ability to work. Twenty-eight months later the blood pressure fluctuated between 165/110 and 150/100. She is considering operation.

Comment.—This is a significant history, because it indicates that in spite of a right-sided hypoplastic kidney, nephrectomy was ineffective and left splanchnic nerve section was more helpful. It emphasizes the point repeatedly made in the literature that nephrosclerosis develops in the opposite kidney which will maintain hypertension. Early nephrectomy, however, may produce a cure of hypertension even in the malignant phase[16] with results lasting from three to five years.

CASE 6.—J. M., 7-year-old girl, entered St. Luke's Hospital on Oct. 15, 1937, because of increasing spells of nausea, vomiting, and headaches.

Past History.—A year previous to entrance, following a choking spell, albuminuria was discovered. Nausea, vomiting, headaches, and restlessness followed a few months later. In June, 1937, she began to have convulsions, with blurred vision lasting two to three days. She had been in bed since that time. Just before entrance she had a series of convulsions.

Entrance.—The child's blood pressure was 190/160. She had a right-sided facial paralysis and was in a comatose state. She received 50 per cent magnesium sulfate and 5 per cent glucose intravenously. Epistaxis and bloody stools were observed. In the next two days her condition greatly improved so that more detailed study could be started. Eye grounds showed bilateral papilledema, retinal hemorrhages, and exudates. Blood pressure fluctuated between 240/190 and 200/150. It dropped to 190/160 on one-third tablet of nitroglycerin. Removal of 50 c.c. of blood would also result in the same lowering of blood pressure. The urine contained hyaline and granular casts; there were 50 mg. of albumin in the urine; 55 per cent of the phenosulfonphthalein dye was excreted in two hours. Concentration-dilution test showed a variation of specific gravity between 1.011 and 1.014. The urea nitrogen was 49.8; the total nonprotein nitrogen 75 mg. per 100 c.c. On a flat plate the left kidney was definitely much smaller than the right. This was confirmed by perirenal air injection.

Diagnosis.—The diagnosis was malignant hypertension due to a unilateral renal disease. The patient was discharged but re-entered on March 7, 1938, in coma. After a critical period she died one month later. Autopsy was refused.

Comment.—This patient was said to have had symptoms for only five months prior to admission. When she arrived at St. Luke's Hospital, and at the time surgical consultation was asked, she was regarded as inoperable because of the high nitrogenous retention. The diagnosis among previous pediatricians was said to be chronic glomerulonephritis. However, unilateral renal disease, amenable to nephrectomy in the earliest, and bilateral splanchnic section in the later stages, was suspected and confirmed by x-ray studies. Whether pyelone-

phritis or congenital aplasia of the kidney was present could not be determined without autopsy.

CASE 7.—P. B., a 7-year-old child, entered the Research and Educational Hospitals on Nov. 27, 1939, on the pediatric service, with complaints of headache, wobbly gait, hematuria, and facial paralysis of several months' duration.

Past History.—The patient appeared to be a healthy, normal infant until about the age of 1 year, at which time she began to have bouts of nausea and vomiting which persisted until admission. There was hematuria, and swelling of the eyelids occurred four to five times in the last twelve months; frequent severe headaches and uncertain gait developed in the last six months. Two months prior to admission the patient suddenly exhibited a right facial paralysis. Since that time the parents also noted dyspnea on exertion, palpitation, and nocturnal dyspnea.

Entrance.—The following positive findings were noted: the blood pressure varied from 226/180 to 188/160 mm. of mercury. There was a right facial paralysis. The right pupil reacted sluggishly to light. The right internal rectus muscle was paretic. The right optic disc was slightly elevated. There was a fan-shaped hemorrhage on the nasal side of the right retina. The left optic disc was slightly blanched with one pin-point hemorrhage. There was angiospasm. The two-meter chest film showed enlargement of the heart to the left; the electrocardiogram revealed questionable evidence of myocardial damage. The urine analysis showed a 3+ albumin. The urine culture showed staphylococci, streptococci, and *Bacillus coli.* The nonprotein nitrogen varied between 31 and 40 mg. per cent. Urine could be concentrated to a specific gravity of 1.020. The phenolsulfonphthalein dye excretion amounted to 70 per cent in two hours. Urea clearance was 18.7 c.c. per minute (24.8 per cent of normal). The intravenous pyelogram showed no concentration of the opaque solution at 10, 20, 30, and 60 minutes. The retrograde pyelogram revealed pyelectasia and dilatation of ureters bilaterally. The spinal tap showed normal chemistry and pressure.

Operations.—On Jan. 30, 1940, a left splanchnic nerve section and removal of the sympathetic ganglionated trunk from the twelfth dorsal to the third lumbar were done. The left kidney showed fetal lobulations. A biopsy was taken, the kidney was decapsulated, and an omental graft was wrapped around it. On Feb. 16, 1940, section of the right splanchnic nerve was done, the kidney was scarified, and a muscle flap sutured into it. On Aug. 6, 1940, a right lumbar sympathectomy from the twelfth dorsal to the third lumbar completed the operation. The postoperative blood pressure was 180/136, 170/130, and 175/140 in the three positions. The patient was asymptomatic after the last operation.

The renal biopsy revealed one portion of the section containing normal glomeruli tubules and interstitial tissue. The lumens of the arterioles were exceedingly small, because of intimal proliferation. There was some recanalization of partially obliterated arterioles. The arteries had hyperplastic media but the lumina were of normal caliber.

In another portion the tissue resembled fetal thyroid; these were undoubtedly remains of kidney tissue since renal tubules were unmistakable. Islands of dense fibrous tissue surrounded delicate tubules with cuboidal epithelium. Some of the tubules were filled with a hyaline-like material. Some of the arteries and arterioles had no lumina being replaced by dense fibrous tissue. The entire picture was consistent with embryonic renal structures with arteriolar obstruction secondary to hypertension.

Course.—The patient was asymptomatic from August, 1940, to November, 1941, at which time she was re-admitted because of recurrent headaches, vomiting, strabismus, burning on urination, dizzy spells, and ataxic gait, all of two weeks' duration. Blood pressure was 190/150 in all positions. The urine culture yielded *Bacillus coli* and Streptococcus *faecalis.* Albumin was 1+, and there were occasoinal red and white blood cells in the urine. The urea clearance was 23.7 c.c. per minute. The patient developed mumps and scarlet fever and was transferred to Cook County Hospital.

On March 19, 1942, two years postoperatively, the patient was readmitted to the pediatric service complaining of recurrent attacks of facial paralysis. The blood pressure varied from 280/250 to 190/110. The arteriovenous ratio in the eye grounds was 1:4 to 1:5; there

were silver-wire arteries and old retino-optic hemorrhage. The urine showed a 4+ albumin (about 3 to 3.5 Gm. daily). There were occasional hyaline and granular casts. She could concentrate urine only to 1.013. Nonprotein nitrogen was from 50 to 72 mg. per cent. The urea nitrogen was 73.3 per cent, and creatinine 2.3 mg. per cent. The electrocardiogram showed only slight deterioration as compared with the one obtained in 1940. She was discharged on April 5, 1942, with a diagnosis of malignant hypertension with impending uremia.

Comment.—This 7-year-old child was operated on in 1940, for bilateral congenital hypoplastic kidneys resulting in a malignant phase of hypertension. She had papilledema and retinal hemorrhages, and did not respond to vasodilators except mecholyl. Her subsequent course downhill, which perhaps was not as rapid as it might have been if she had not been operated upon, showed a gradual progression of the renal damage to terminal uremia. The onset of the lesion and the findings of the biopsy leave no doubt that a congenital hypoplasia of renal tissue was responsible for the hypertension. At the age of 7 years, when the condition was first recognized, the hypertension was in a malignant phase and inoperable according to our present indications. Nephrectomy was not feasible, first because both kidneys were involved with a superimposed pyelonephritis and second because the arteriolar lesion had injured the other kidney. Certainly a recognition of such a lesion at the age of 1 or 2 years instead of at the age of 7 might have given this child a better chance.

Hypertension Following Renal Trauma.—Two patients in this series had a history of severe trauma to the region of the kidney, followed by hematuria, and exhibited deformed renal calices or decrease in the size of the kidney. Whether the trauma is a factor in their hypertension is debatable. However, we have grouped these two patients together, since their history and their reaction to surgery was so similar.

Case 8.—J. A., a 31-year-old grain dealer, was admitted to St. Luke's Hospital on May 19, 1943, stating that he knew of his high blood pressure; however, he had no symptoms referable to it.

Past History.—In high school he had been kicked in the right flank after which he went into shock and had blood in the urine. About ten years before entrance he suffered from malaria for two years. Five months before entrance, on physical examination from the Army, he was told that he had a blood pressure over 200 mm. of mercury. Local physicians had obtained pressures between 200 and 150 mm. of mercury. His mother had died at 60 years of age of a stroke; his father had died at 56 of a heart attack; one brother, aged 52, had high blood pressure.

Entrance.—The patient's blood pressure was 210/134. Physical examination revealed a diffuse enlargement of the thyroid gland, especially on the left. There was a soft systolic murmur at the apex and an occasional faint splitting of the first sound. The eye grounds showed moderate spasm of the retinal arteries with some arteriovenous compression; the retinopathy was grade 2. The heart occupied 59 per cent of the thorax; the left ventricle seemed slightly enlarged. Electrocardiogram showed evidence of myocardial damage with the first and second thoracic inverted, the third thoracic low and the S-T segment elevated in Lead IV. The basal metabolic rate was −8 per cent. The intravenous pyelogram revealed some dilatation of the ureter, sharply localized just below the sacroiliac joint and the displacement of the right ureter in its mid-portion toward the midline. The urine was negative. The kidneys concentrated from 1.003 to 1.024. The urea clearance was 82.5 c.c. (standard). Blood chemistry was normal. The response to ice water was from 194/136 to 240/180 mm. of mercury; sodium amytal depressed the blood pressure from 172/134 to 140/100.

Operations.—Operations were done on May 26, 1943, and Oct. 11, 1943. Since he had a stitch abscess after the right splanchnic nerve section, he was discharged and the left side operated on five months later. Blood pressure, six months after the completion of the second operation, was 140/105, 150/105, and 145/105 in the three positions. The specific gravity of the urie was 1.030. He was asymptomatic, but after one week of steady drinking the pressure was 180/110. One year after the completion of the second stage the blood pressure was 130/84 in all positions. Two years after the operation he was asymptomatic, working full time, with a blood pressure of 130/80 mm. of mercury.

Comment.—This patient had a bad family history; whether the trauma to the right kidney accelerated the appearance and progress of the hypertension is open to debate. The vasomotor reactivity was exaggerated. He had kinks in both ureters, perhaps due to strictures and early pyelonephritis. The combination of these factors, however, produced a severe hypertension in a man of 31 years; the operation up to the time of this report has been definitely beneficial. Note that the preoperative basal blood pressure (under 9 gr. of sodium amytal) corresponds to the postoperative pressures at six months, but that he continued to improve later.

Case 9.—L. F., a 17-year-old boy, entered the Research and Educational Hospitals on Aug. 13, 1941, complaining of occasional frontal headaches, fatigue for the past eighteen months. An elevation of blood pressure was discovered four months before.

Past History.—The patient had an injury to the right side at the of age 9 years, resulting in internal hemorrhage and hematuria. He had always been active; one grandmother had hypertension.

Entrance.—Physical examination was negative except for a blood pressure of 190/120. The eye grounds revealed slight angiospasm. The electrocardiogram showed changes compatible with left heart strain. The heart in the two-meter chest film occupied 50 per cent of the thorax. The urinalysis showed an occasional red blood cell, cast, and slight albuminuria. The urea clearance was 58 c.c. (maximal). The phenolsulfonphthalein dye appeared in 40 per cent concentration in fifteen minutes. Concentration was possible to 1.025. The inulin clearance was 118 c.c.; the diodrast clearance was 574 c.c. per minute. The pyelogram showed an unusual deformity of the right renal pelvis. Blood chemistry was within normal limits. Ice water raised the blood pressure from 188/120 to 210/140. Sodium amytal depressed it from 210/110 to 168/100 mm. of mercury. Epinephrine raised it from 212/138 to 300/176 mm. of mercury.

Operations.—Bilateral dorsolumbar sympathectomy and splanchnic nerve sections were done on Jan. 13, 1943, and Oct. 11, 1943. On discharge the blood pressure was 132/90, 130/90, and 90/50 mm. of mercury.

Course.—Three months later the blood pressure was 150/100, 130/90, and 120/80 mm. of mercury. There were no complaints. Six months later the blood pressure was 150/100, 142/90, and 148/90 in the three positions. He was working full time and felt well. One year later the pressures varied between 140/90 and 124/84 mm. of mercury in the horizontal position. Electrocardiogram showed improvement compared with the preoperative one.

Comment.—Again there is increased vasomotor reactivity, history of a renal injury, and severe juvenile hypertension. The blood pressure under sodium amytal was 168/100 before the operation; the blood pressures six months following operation were from 150/100. One year after the operation the blood pressure was 140/90. Three years after the operation the blood pressure was 135/90.

Post-toxemic Hypertension.—Our present knowledge concerning pre-eclamptic and eclamptic toxemia of pregnancy has been summarized and extended

by the monograph of Dexter and Weiss.[17] We quote: "Sustained hypertension follows toxemia of pregnancy in about one-quarter of the patients who had normal blood pressure before pregnancy. It is not so much the severity but the duration of the toxemia which is responsible for the persistent hypertension."

The main histologic changes are found in the placenta, liver, kidney and retina. Renal changes specific for toxemia were described by Fahr as glomerulonephrosis.[18] There is evidence that in toxemia a generalized damage of the capillary endothelium exists. The clinical effect of this is a type of hepatorenal syndrome with cerebral manifestations.

The renal lesion secondary to toxemia is an example of a state in which endogenous factors, such as originate in the placenta, liver, or glands of internal secretion, produce structural arteriolar changes in the kidney which in turn may produce renal ischemia and the liberation of pressor substances producing hypertension. It would seem that the incidence of post-partum hypertension may be greatly curtailed by not allowing toxemia to persist more than three weeks during pregnancy.

Some of the case histories to be presented are a sad commentary on the indifference or carelessness of some obstetricians. If the toxemic injury to the kidneys lasts too long, or if repeated toxemias are allowed to persist, a malignant hypertension may be the result. But with a single injury, which subsides and does not continue to damage the kidney, the results have been very favorable. The resulting nephrosclerosis yields to our surgical approach and some of our best results have been in patients with grade 2 hypertension of this group.

CASE 10.—A. S., a 33-year-old housewife, was admitted to Research and Educational Hospitals on March 2, 1942, complaining of dyspnea on exertion, frequent headaches, dizziness, precordial pain on exertion, and palpitation for the past twelve months.

Past History.—The patient was told of an increase in blood pressure one year before, when she was in the seventh month of pregnancy. Previous pressures were normal. She was placed at bed rest until after delivery, which was normal. She had two previous uncomplicated pregnancies. Her mother had died in the early forties of high blood pressure.

Entrance.—Blood pressure was 166/110 mm. of mercury. Physical examination was essentially negative. Eye grounds revealed angiospasm of retinal vessels with an arteriovenous ratio of 1:4 and slight nicking. Heart was moderately enlarged on x-ray examination. Basal metabolism was +9 per cent. Concentration of urine was possible to 1.030. The phenolsulfonphthalein dye was excreted up to 30 per cent in fifteen minutes and 58 per cent in one hour. Urea clearance was 48 per cent (standard). The intravenous pyelogram was normal. Sodium amytal depressed the blood pressure to 122/80 mm. of mercury; ice water raised it from 140/100 to 160/122 mm. of mercury.

Operations.—Operations in two stages was done on April 14 and 28, 1942. On discharge the pressure was 142/96, 128/92, and 84/56 in the three positions.

Course.—One and one-half years later she complained of an occasional headache, no dizziness or fatigue. The headaches were premenstrual. She worked all day. The pressure was 120/85, 118/85, and 122/85 mm. of mercury in the three positions. Two and one-half years later the pressure was 120/80 in all three positions.

Comment.—The toxemia in this patient lasted for the last two months of pregnancy. The post-toxemic hypertension had persisted for only one year before operation. The vasomotor relaxation resulted in a normal blood pressure.

Under such favorable conditions a restoration of blood pressure to normal was accomplished. Further pregnancies should not be permitted.

CASE 11.—M. C., a 35-year-old married woman, entered St. Luke's Hospital on Dec. 15, 1940, complaining of hives and edema of face, wrists, and ankles since the age of 17; headaches, dizziness, and palpitation of at least twelve years' duration.

Past History.—The patient had had emotional urticaria and edema since the age of 17. They were not demonstrably caused by foods, cosmetics, or seasonal variations. In 1928, during the first pregnancy, hypertension was discovered. She had a great deal of nausea, vomiting, and edema, and in the eighth month she had nine severe convulsions with anuria for four days. A cesarean section was performed and a dead infant delivered. She seemed fairly well until 1934 when following a "head cold," nausea, vomiting, and generalized edema returned. Again she was anuric. In 1936 the headaches stopped. During the last few months before admission she felt increasingly fatigued, sleepy, and noticed dizziness on walking.

Entrance.—The fundi showed arteriolar spasticity, arteriovenous nicking but no retinal hemorrhages or exudates. The blood pressure varied from 210 to 146 systolic and 140 to 96 diastolic. The lowest pressure under sodium amytal was 132/88. The cold pressor test raised the blood pressure from 150/100 to 186/110 mm. of mercury. The heart occupied 53 per cent of the thorax. Electrocardiogram showed minimal myocardial damage. The basal metabolism was +9 per cent. Urea clearance, concentration-dilution, and phenolsulfonphthalein elimination were within normal limits. A diagnosis of posteclamptic hypertension, grade 1, was made.

Operations.—Operations were performed on Dec. 16 and 26, 1940. A *bacillus coli* pyelitis followed the second stage. Renal biopsy revealed chronic glomerular, tubular, and interstitial damage. She was discharged with a blood pressure of 114/80 in the horizontal position.

Course.—The patient began to gain weight. The previous restlessness disappeared. Postural hypotension (60/0) was marked for six weeks, after which it caused no complaints. It was absent after three months. Up to thirty-six months after operation the blood pressure varied from 120 to 105 systolic and 86 to 75 mm. of mercury diastolic pressure. At the last examination, three and one-half years after the operation, blood pressure was 150/90, 140/100, and 120/84 in the three positions. However, she suddenly lost her eyesight and a tentative diagnosis of cerebral aneurysm at the base of the brain was made.

Comment.—This patient had a history of toxemia of pregnancy with convulsions; she also had a marked vasomotor instability as manifested in the emotional urticaria and edema. An excellent control of blood pressure was obtained for three and one-half years; whether the vascular lesion at the base of the brain is a congenital or an arteriosclerotic weakening of the vessel wall is impossible to determine. At this time she is almost completely blind, with a normal blood pressure. The symptoms date back twelve years.

CASE 12.—K. de T., a 30-year-old housewife, was admitted to St. Luke's Hospital on June 22, 1941, complaining of severe headache and dyspnea on exertion for two years. She had an attack of numbness on the entire left side with inability to walk which lasted one to three days, ten months previous to entrance.

Past History.—Ten years previously she had a toxemia of pregnancy. The pregnancy was not terminated and she has one healthy child. Her blood pressure was normal before and during the first trimester of pregnancy. Her mother had died in an uremic state and her father had died of a stroke.

Entrance.—The patient's blood pressure was 200/120 mm. of mercury. Physical examination was essentially negative. Eye grounds revealed a generalized arterial constriction with an occasional white exudate. The heart occupied 46 per cent of the thorax; the

electrocardiogram showed no diagnostic deformities. She concentrated and diluted urine between 1.019 and 1.002; the dye was excreted to 10 per cent in fifteen minutes. Urea clearance was 59.4 c.c.; blood chemistry was normal, as was the intravenous pyelogram. Sodium amytal depressed the blood pressure from 196/122 to 166/118 mm. of mercury. Ice water raised the pressure from 189/123 to 236/170 mm. of mercury.

Operations.—Bilateral dorsolumbar sympathectomy and splanchnic nerve section were done on June 27, 1941, and July 11, 1941. The kidney felt hard and small, and whitish scars were on its surface. The second stage was followed by pneumothorax and pleural effusion, but no delay in convalescence. She left the hospital on July 27, 1941, with the following blood pressure: lying down, 145/100; sitting up, 90/60; standing, 80/0. The renal biopsy showed hyaline, shrunken glomeruli, thickened vessel walls: a marked nephrosclerosis.

Course.—The patient was re-examined every three months the first, every six months the second year. On Nov. 15, 1943, two years postoperative, the pressure was 160/115 in the horizontal, 140/110 in the sitting, and 130/110 in the standing position. Urine showed no pathologic elements; the specific gravity was 1.015. She had no headaches or dizziness, had occasional palpitation, but felt very listless. On April 11, 1945, the pressure rose to the preoperative level.

Comment.—This patient had a normal blood pressure before pregnancy Family history for cardiovascular renal disease was unfavorable. She had generalized edema in the fifth month of pregnancy. She was operated on for a grade 2 hypertension with irreversible renal damage, with poor response to barbiturates, and an excessive response to ice water. Four years after operation both the symptoms and the actual blood pressures were close to where they were prior to operation. While she had four years of comfort and the process seemed to have been arrested, there is now a recurrence of the hypertensive state. In retrospect the following observations might point to such a course: (1) Under sodium amytal the minimum pressure obtained was 166/118, the diastolic being somewhat higher than we like it to be; (2) the concentration test showed values up to 1.019, the phenolsulfonphthalein excretion in fifteen minutes was only 10 per cent. On the other hand, the urea clearance was comparatively high: 59.4 c.c.; (3) during anesthesia the blood pressure did not drop very much and stayed around 160/120, indicating as the operative note stated that "organic damage was considerable"; (4) inspection and palpation of both kidneys revealed small, hard, shrunken kidneys showing small white depressed scars on the surface.

In addition, the patient's married life had been unfortunate, ending in divorce and remarriage. She was restless, unhappy, and had avoided all responsibility in both of the marriages. The last examination almost four years after the operation revealed a recurrence of symptoms and return of the blood pressure levels to a slightly lower than preoperative level. One lumbar chain was not completely severed. The renal damage was too great. These two factors were held responsible for the recurrence.

CASE 13.—H. F., a 23-year-old housewife, was admitted to St. Luke's Hospital on May 11, 1942, complaining of nervousness for six years; severe headaches for two years; "strokes" one and two years before admission, with transient aphasia and paralysis of left and right upper extremity for four to six weeks each time; coldness of lower extremities and occasional hematuria.

Past History.—The patient was perfectly well until six years before when she became very nervous. Five years before she had a severe toxemia of pregnancy with convulsions and generalized edema for the entire third trimester. The infant was stillborn. While the patient had scarlet fever at the age of 9, which left her with a discharging ear, she had no kidney trouble and the blood pressure was not elevated before the pregnancy. The family history was not contributory.

Entrance.—The patient's blood pressure was 135/90 mm. of mercury. Physical examination revealed a slight left lumbar tenderness and residual weakness and spasticity of both arms and hands. There was left facial weakness. Eye grounds revealed a slight bitemporal pallor of the discs. The heart occupied 42 per cent of the thorax; electrocardiogram showed evidence of myocardial damage. She concentrated urine to 1.022 and diluted to 1.002; excreted the dye to 20 per cent in fifteen minutes. The urea clearance was 74.4 c.c. (standard). There was persistently more than 50 mg. of albumin in the urine. The intravenous pyelograms were normal, but there were some calcified spots to the right and left of the midline suggestive of calcification in the suprarenal glands. There was some old infiltration in the upper portion of the right lung, which appeared to be well organized. Sodium amytal depressed the blood pressure from 130/94 to 100/80 mm. of mercury. On immersion into ice water the pressure rose from 135/90 to 140/96; epinephrine raised the blood pressure from 130/90 to 190/100 mm. of mercury. The impression was that of a posteclamptic hypertension resulting in diffuse arteriolar disease. The diastolic pressure was consistently above 90 mm. of mercury, but the systolic was low owing to myocardial damage or possibly damage to the adrenal glands.

Operations.—Operations were performed on May 20, 1942, and June 8, 1942. Following the first stage the patient exhibited a temperature of 104.6° F., a slow pulse and respiration, and a marked mottled peripheral cyanosis. This was thought to be a cerebral vascular accident in the midbrain or a Waterhouse-Friderichsen syndrome which fortunately subsided in three days. The second stage was performed nineteen days after the first one without any unusual complication. The kidneys were small and firm and both adrenals were also visualized; while the adrenals felt smaller and more nodular than normal, there was no evidence of tumor or calcification on palpation. The renal biopsy taken from the right kidney showed marked fibroplastic changes; there were wedgelike sections of cellular fibrous tissue, which extended deep into the parenchyma. Here the tubules and glomeruli had undergone marked retrogressive changes. There were clusters of atrophic glomeruli reduced to masses of hyaline material and the tubules had disappeared almost completely. There were also lymphocytes with small residues of tubule cells. There were various stages of involution but outside these wedges the tubules contained columnar lining cells and the lumens were filled with granular precipitates. The glomerular tufts in these portions were also cellular and had considerable fibrous stroma. The large blood vessels included in the scarred portions had very narrow lumens and intimal fibrous tissue thickenings, but the blood vessels elsewhere also had thick muscular walls with some fibrous thickening along the intimal edge. The interpretation of these findings was that nephrosclerosis was the main tissue change.

Course.—When the patient left the hospital on Aug. 19, 1942, the blood pressure was 112/86. The epinephrine sensitivity decreased. She was re-examined on July 3, 1943, with a blood pressure of 110/70 in the horizontal, 100/70 in the standing position. She felt well and used the paralyzed arm more freely.

Comment.—This was a frail, constitutionally inferior patient who received a severe vascular lesion during pregnancy. Whether there was a latent adrenal insufficiency present was uncertain and it was not feasible to test her for this. The cerebral, cardiac, and renal lesion might have been embolic in nature originating from a subacute bacterial endocarditis but this suggestion, made by our medical consultant, could not be confirmed or disproved. While the weakness and easy fatigability persist to this time, the blood pressure has remained

TABLE II. CORRELATION OF CLINICAL GRADES OF HYPERTENSION WITH RENAL HISTOLOGY

GRADES	NUMBER OF CASES		REMARKS
	CLINICAL	RENAL	
1	10	14	4 patients with grade 2-3 hypertension had grade 1 renal changes
2	13	9	4 patients differed, the biopsy always showing less advanced changes
3	7	7	1 malignant case had a grade 1 renal biopsy 1 patient with grade 2 hypertension showed grade 3 histologic changes

normal for three years and she can do her own housework. The diagnosis of posteclamptic hypertension is still the most likely.

THE PYELONEPHRITIC HYPERTENSION.—In their monograph on the relation of pyelonephritis to hypertension, Weiss and Parker[19] made the important point that the severity and diffuseness of the vascular lesion in this disease is closely related to the degree of hypertension. Patients with severe hypertension had advanced hyperplastic arteriolosclerosis, productive endarteritis, and necrotizing arteriolitis in the kidney. They also stated that pyelonephritis is responsible for at least 15 to 20 per cent of cases of malignant hypertension.

This is in contrast to many statements in the literature that patients with pyelonephritis do not have a higher incidence of hypertension than those of a similar age group without pyelonephritis. However, such collective statistics miss the evaluation of the individual severity of the lesion, whether the pyelonephritis is acute, chronic, recurrent, or healed. Early in our studies of renal biopsy material it was found that the so-called essential hypertension, with no history and no urinary findings of a pyelonephritis, may reveal a renal histology consistent with a latent or healed pyelonephritis. The differential diagnosis between the vascular changes in pyelonephritis and nephrosclerosis has been discussed in detail in another communication.[3] Here only a table is reproduced (Table III).

CASE 14.—A. B., a 33-year-old housewife, was admitted to St. Luke's Hospital on May 20, 1941, complaining of fullness of head and face and weakness for two years, obesity for past few years, and transient edema of eyelids and ankles for the past two years.

TABLE III. DIFFERENTIAL DIAGNOSIS OF VASCULAR LESIONS IN PYELONEPHRITIS AND NEPHROSCLEROSIS

VASCULAR LESION IN	PYELONEPHRITIS	NEPHROSCLEROSIS*
Arteries	Productive endarteritis (basophilic reticular tissue) Reduplication of internal elastic membrane Medial hypertrophy	Internal thickening due to acidophile, dense connective tissue, and hyalinization Splitting and reduplication of the internal elastic membrane
Arterioles	Concentric proliferation of cells with increase in collagen Hyperplastic arteriolar sclerosis Hyaline degeneration only in the older group	Hyaline degeneration

*The malignant phase produces changes identical with those seen in pyelonephritis, that is productive endarteritis and hyperplastic arteriolar sclerosis.

Based on the monograph of Weiss and Parker.[19]

Past History.—Two years previous to entrance the patient noticed puffiness of the eyelids and ankles. She received treatment for this and the symptoms subsided. She became pregnant in December, 1940, and noticed a recurrence of symptoms. She aborted at this time after which the symptoms improved, but only temporarily.

She had the usual diseases of childhood, a cholecystectomy in 1936, and the previously named abortion in 1940. Her father died of "heart trouble" at the age of 50 years.

Entrance.—The patient's blood pressure was 210/120. Physical examination was essentially negative. She weighed 210 pounds. Eye grounds showed a grade 1 hypertensive retinopathy. The heart occupied 43 per cent of the thorax. The electrocardiogram showed no diagnostic deformities. She concentrated urine to 1.033, diluted to 1.004. The urea clearance was 62.5 (standard). Blood chemistry was within normal limits including blood cholesterol. The basal rate was +16 per cent. Sodium amytal depressed the blood pressure from 166/94 to 134/82. The cold pressor test raised it from 148/90 to 180/115. On bed rest the blood pressure fluctuated between 210/120 and 158/110.

Operations.—Operations were done on June 30, 1941, and July 14, 1941, after an intensive reducing therapy which resulted in the loss of thirty pounds. Postoperative course after each stage was followed by a rise in temperature and lumbar ache, but no diagnosis of acute pyelonephritis could be made. The patient left the hospital on June 24, 1941, with a blood pressure of 138/80 in the horizontal position. A postural hypotension was not recorded. The renal biopsy recorded small focal infiltrations of lymphocytes and plasma cells. In these places the tubules were distended and contained granular precipitates. The glomeruli had prominent vascular tufts; some had hyaline changes and were shrunken.

Course.—The patient returned one year later on June 8, 1942, with an acute severe pyelitis and degenerating fibroids of the uterus. The blood pressure at bed rest was 140/90. In July, 1942, she had a panhysterectomy with uneventful recovery. The blood pressures were never above 140/95 during the period of hospitalization. Following hysterectomy, weight rose from 190 pounds to 210 pounds. On Nov. 3, 1943, two and one-half years after the operation, she complained of recurring headaches. The blood pressure was 186/130 mm. of mercury in the horizontal and 196/130 in the standing position. The lower extremities showed sweating in the distribution of the second and third lumbar. The last inquiry recorded blood pressures of 200/140 in the sitting position and 188/144 lying down. The headaches were still bothersome and she was still overweight.

Comment.—The history, the renal biopsy, and the subsequent course of this patient justify a diagnosis of chronic recurrent pyelonephritis with secondary vascular damage. That the lesion had not healed is demonstrated by the recurrent attacks of chill and pyuria. In addition, the sympathetic denervation was not as complete as we would prefer it to be since the second lumbar ganglia seem not to have been inactivated. There is nothing to justify the assumption that splanchnic section would be effective in cases of active or reactivated stages of pyelonephritis. In fact, such cases may head toward the malignant phase.

However, in Case 15 a better result is shown in a case of healed pyelonephritis with severe hypertension.

CASE 15.—G. P., a 33-year-old white truck driver, was admitted to the Research and Educational Hospitals on Oct. 21, 1940, complaining of headaches and blurring of vision for the preceding ten months and of palpitation for the preceding three weeks.

Past History.—He was well until ten months before entrance, when he had a period of *nycturia* for several days. Examination of the urine revealed albumin. He had some vomiting and a slight fever at this time. A diagnosis of renal infection was made. This acute episode subsided in a few weeks. The patient's father died of heart disease and one sister of Bright's disease.

Entrance.—The blood pressure was 220/140 mm. of mercury. Physical examination revealed evidence of some recent weight loss, slight emphysema of the chest, and an enlargement of the heart to 1 cm. to the left of the midclavicular line. The eye grounds showed an early grade 3 hypertensive retinopathy. An electrocardiogram revealed left ventricular preponderance. The basal metabolic rate was −1 per cent. He was able to concentrate urine to 1.038. The phenolsulfonphthalein test showed 25 per cent excretion in the first fifteen minutes. The urea clearance was 47 c.c. (standard). The intravenous pyelogram showed poor filling of the left pelvis. No retrograde pyelogram was done. The urea nitrogen was 19, the nonprotein nitrogen 38, giving a *urea ratio of 50.* Sodium amytal depressed the blood pressure from 206/124 to 160/114, sodium nitrite from 202/118 to 156/108, and intravenous pentothal from 180/130 to 122/92. Ice water modified the pressure from 188/134 to 172/120, an inverse reaction.

Operations.—Operations were performed on Dec. 8, 1940, on the right and three weeks later on the left side. Blood pressure when the patient left the hospital was 160/100 in the horizontal, 154/108 in the sitting, and 102/88 in the standing position. Renal biopsy was reported to be consistent with chronic pyelonephritis.

Course.—One month after discharge the patient was able to sleep without sedatives and had only a few headaches. He still had some precordial discomfort. The blood pressure was 180/128 in the horizontal position. Six months later he was back at work with a pressure of 160/100 in all positions. Examined four years postoperatively, blood pressure was 150/100 in all three positions. He could work eight hours daily but felt tired at the end of the day and had occasional headaches.

Comment.—Compared with the considerable organic damage which this patient exhibited before the operation, the postoperative course has been quite favorable. This was a grade 2 hypertension originating from a pyelonephritis.

STREPTOCOCCUS NEPHRITIS FOLLOWED BY HYPERTENSION.—It is sufficiently known that the nephritis following scarlet fever or streptococcus infections may give rise to a persistent hypertension. That such a nephritic hypertension responds to sympathectomy is illustrated in Case 16.

CASE 16.—J. G., a 15-year-old white boy, entered the Research and Educational Hospitals on Feb. 12, 1941. He had no complaints.

Past History.—This boy had always been well and had no difficulty other than some social maladjustment. Five years previous to entrance, at the age of 10 years, he had erysipelas of the face complicated by renal involvement. During this time he had blood, hyaline, and granular casts in the urine and the blood pressure rose to 180/120 mm. of mercury. A physical examination done six months before entrance disclosed a blood pressure of 160/100 mm. of mercury for which reason he was referred to the University Clinics.

Entrance.—The patient's blood pressure was 175/125 mm. of mercury. The fundi seemed normal. The examination of the heart revealed an old rheumatic mitral valvulitis. The electrocardiogram was consistent with an old rheumatic heart disease. The two-meter chest film showed the heart and great vessels to be of normal size. The urine showed an occasional cast and a trace of albumin. The urine could be concentrated to 1.026. The dye was excreted to 30 per cent in fifteen minutes and the urea clearance was 40 c.c. (standard). Sodium amytal depressed the blood pressure from 160/110 to 125/80, the ice water raised it from 145/90 to 160/100, epinephrine raised it from 160/95 to 190/90. On bed rest the lowest pressure obtained was 145/90.

Operations.—Operations were performed on June 24, 1941, and July 1, 1941. The postoperative course was uneventful. The blood pressure on discharge was 110/72 lying, 70/50 sitting and 50/38 in the standing positions. Unfortunately no renal biopsy was available.

Course.—Two months postoperatively the patient had no complaints of any kind and was working as a waiter. A blood pressure in the sitting position was recorded to be 118/80.

No further visits to the Dispensary are recorded since he was inducted into the Army in the same year (1941). Information received from his father in October, 1943, revealed that he had been on active duty in Alaska for two years and had no complaints. Efforts to obtain a blood pressure reading have so far failed.

Comment.—The sequence of erysipelas followed by hematuria and hypertension make the diagnosis of a streptococcus nephritis most likely. This may well be a vascular type of sensitization as Andrews, Derick and Swift,[20] and Rich and Gregory[21] have postulated. The effect of splanchnic nerve section on this lesion was gratifying.

The Rheumatic Hypertension.—In a short, mostly ignored communication Fahr[22] stated that the rheumatic infection may produce a malignant, not arteriolar sclerotic type of nephrosclerosis. In this country the studies of Taussig and Hecht[23] have shed important light on the subject, although neither pediatricians nor internists seem to have recognized the importance of these statistical studies. They first described three cases in which during the course of rheumatic fever hypertension developed under observation; nephritis or other causes of hypertension were excluded. Next they studied the histories of 500 rheumatic children; forty-nine of these had hypertension. While they stated that the exact relation between the hypertension and the rheumatic infection was unclear, again no children with nephritis or with other obvious causes for hypertension were included.

We wish to present a few cases from our surgical material and one final one observed on the medical service of the Research and Educational Hospitals which would indicate the comparative frequency of this lesion and their responsiveness to surgical treatment.

Case 17.—J. W., a 24-year-old white man, entered the Research and Educational Hospitals on April 23, 1942, complaining of weakness, dyspnea on exertion, and palpitation of three months' duration.

Past History.—The patient had had rheumatic fever at the age of 12 years and associated arthropathy with a recurrence at the ages of 16 and 17. At the age of 19 he showed some ankle edema. In 1941, at the age of 23, he developed another attack which kept him in bed off and on until his entrance to the hospital. There were no other diseases and the family history was negative except for one brother with hypertension.

Entrance.—The patient's blood pressure was 158/90. The heart was of normal size on physical examination and on a two-meter chest film. There were, however, a palpable thrill and a loud systolic murmur at the apex of the heart. Funduscopic examination revealed a grade 1 hypertensive retinopathy. The electrocardiogram showed the presence of mitral heart disease. The basal metabolic rate was –2 per cent. Blood chemistry was normal. The urine could be concentrated to 1.034; 10 per cent of the dye was excreted in the first fifteen minutes. The urea clearance was 37 c.c. (standard). The intravenous pyelogram was normal. The inulin and diodrast clearances were within normal limits. Under sodium amytal the pressure dropped from 160/90 to 118/80; sodium nitrite lowered the pressure from 140/90 to 122/80. Ice water raised the pressure from 154/98 to 184/126. Epinephrine raised the pressure from 160/92 to 180/90.

This was a grade 1 hypertension in a 24-year-old individual with rheumatic heart disease and operation was advised.

Operations.—Operations were performed on July 14, 1942, and July 23, 1942. The postoperative course was uneventful. On discharge the pressure in the horizontal position was 138/90, sitting 130/90, and could not be obtained on standing. No data were available as to the level of sweating. Renal biopsy showed hyperplastic arteriolar sclerosis and productive endarteritis.

Course.—Six months postoperatively the patient was working eight hours a day; he complained of fatigue but less dyspnea. Blood pressure was 146/82 lying down, 140/80 sitting, and 120/80 standing. As a hotel clerk he stood most of the time. One year after the operation blood pressure was 140/80 in all positions; he of course still had the symptoms of not entirely compensated mitral heart disease. Three years after operation blood pressure was 138/80.

Comment.—This was a patient with a history of rheumatic infection, a rheumatic heart, and a hypertension of vascular origin showing hyperplastic arteriolar reaction in the absence of pyelonephritis. These findings seem more than coincidental.[23]

CASE 18.—J. W. M., a white girl aged 15 years, unmarried, was admitted to the cardiac clinic of the University Dispensary on Oct. 15, 1938 and then to the Research and Educational Hospitals on November 8, 1938 complaining of shortness of breath, palpitation, tremor, nervousness, and weight loss of five months' duration.

Past History.—Eight years previously, at the age of 7, the patient had chorea and "heart trouble" which responded satisfactorily to bed rest. She was normally active for the next seven and one-half years. Five months prior to entrance she developed a violent attack of palpitation followed later by "trembling." Later a weight loss occurred in spite of an adequate appetite. Two weeks before admission attacks of dyspnea occurred independent of the tremor or palpitation. Her father died of pulmonary tuberculosis at the age of 38. Her mother has an arrested case of tuberculosis; she had had a thoracoplasty.

Entrance.—The patient's blood pressure was 168/120 mm. of mercury. The heart was enlarged to the left. The first mitral sound was replaced by a short systolic murmur. The pulmonary second sound was louder than the aortic second. Two-meter chest film showed an increase in the hilus shadow with considerable calcification suggesting an old tuberculosis. The basal metabolic rate was 9 per cent. Blood chemistry was within normal limits. Urea clearance was 45 c.c. (standard). The cold pressor test showed a maximum systolic rise of 24 mm., a maximum diastolic rise of 46 mm. of mercury. Intravenous sodium pentothal lowered the pressure from 184/138 to 126/94. She was discharged on Nov. 23, 1938.

The second hospital admission occurred on Feb. 20, 1940. Added complaints on this admission included precordial pain and orthopnea for one month. Blood pressure at bed rest was recorded as varying from 140/110 to 158/120. A psychiatric consultation was requested and conferences were arranged.

Summary of Psychiatric Interviews.—Psychotherapeutic interviews took place twice weekly from March 23, 1940, to May 23, 1940, a total of seventeen hours. During this period, the patient reported only one nocturnal anxiety attack. Blood pressure readings were made during about half of the visits at about ten-minute intervals. The range of systolic pressures was 144 to 174, most of the readings falling between 150 and 160. Even in the presence of acute anxiety the systolic pressure did not rise above 174. The diastolic pressure varied from 108 to 136, the usual readings being between 120 and 130. The systolic pressure was more labile than the diastolic pressure and appeared to fluctuate under the influence of emotion. Thus, when the patient was apprehensive about the material under discussion, the systolic level ascended to the region 170. When her fears were allayed by reassurance, the level fell to 150 or lower. Diastolic pressure, however, remained relatively fixed.

The patient proved to be cooperative in the interviews and showed willingness to deal with the materials brought up by the interviews. Her fear of unrecognized tendencies in her personality made progress slow. From the interviews as well as from a social history obtained from the mother and the sister, an opinion may be ventured about the psychologic side of the case. The striking fact is the discrepancy between a sensitive and highly vulnerable make-up, and inhibition of expressive feeling. On the one hand the patient had always been easily stirred emotionally, and on the other hand she had never been known to release angry feelings. In working with the materials of her life, one gained the impression that she had stored up an immense amount of hostile feeling; yet, she had the reputation

for being a very gentle and soft-spoken person. This contrast was exhibited in her behavior during the interviews. Although appearing calm and well poised, she reacted very sensitively to any remark bearing on her personal problems and obviously struggled for control of her emotions. It seemed that the accumulation of unhappy emotion over the years was related to the hypertension. The energy of the emotion being blocked in expressive behavior, it found an outlet in the vascular system.

The origin of the hostile reactions and of the need to suppress them require rather lengthy discussion for their elucidation. In a word, it may be stated that the hostilities arose out of rivalry with mother and sister and a protective response to the consistently aggressive behavior of the sister. The inhibition of frank emotional response was due to fear of punishment. The latter was associated with many fantasies of punishment animated by experiences of an everyday kind. The constant evocation of these fantasies made expression of emotion dangerous, and filled the patient with anxiety. One of her punishment fantasies was sudden death by reason of heart failure, this fantasy having grown out of the diagnosis "leakage of the heart" made in childhood. It was this fantasy which appears to have been responsible for the anxiety attacks at night. Reassurance on this point may have played a role in eliminating the attacks. Another punishment fantasy consisted of being mutilated. Under the influence of this fantasy, the patient had for years dreaded an operation as a punitive procedure. The impending operation of sympathectomy caused a great deal of anxiety, reflected in the rise of the systolic level to about 200 following admission to the hospital.

The psychotherapeutic aim in this case was to bring about a release of the repressed emotion by removing the fears that blocked its expression. This process of desensitization necessarily required a long period of psychotherapy. During the course of treatment, blood pressure levels sometimes rose as the result of the emergence of fear. Ultimately, however, if the hypothesis of a relationship between hypertension and repressed emotion was correct, release of the emotion should have brought about a lowering of the blood pressure. Even if sympathectomy were successful, the patient should continue under psychiatric care because the emotional tension did not find release in some other bodily mechanism. And apart from the threat to health, the patient required insight and guidance in improving the general adjustment.

Comment.—There are several reasons for giving this patient's history in more detail. She had a good history and clinical evidence for a rheumatic infection. She seemed to be suitable for sympathectomy since she belonged to group 1. The psychiatric interviews disclosed an interesting light on her personality but the seventeen weekly conferences had no effect on the blood pressure and her renal function had meanwhile deteriorated. Blood pressure became normal after bilateral splanchnic nerve section undertaken on June 6, 1940, and July 23, 1940. She became pregnant one and one-half years later but the pressure remained normal until the last month, at which time it rose to 170/120. She gained thirty-five pounds during the pregnancy but no albumin was recorded in the urine. However, when discharged from the obstetrical service on the twelfth day, blood pressure was 130/96. Four years after the sympathectomies and two and one-half years after delivery, blood pressure was 150/90 in all three positions. It was thought that denervation of the second and third lumbar segments might help and therefore additional lumbar sympathectomies were done with the result that pressures are normal at the time this paper was written. She went to work as a truck driver, and seemed completely adjusted and content.

In this case there seemed to be several factors operating: the rheumatic, the psychologic, and the pregnancy factor. It is open to question whether she

should have been allowed to become pregnant. The additional load seemed to have initiated the recurrence of the hypertension for which additional sympathetic denervations were done. In our opinion she should never become pregnant again.

Fig. 3.—Nitrogenous retention and rise in blood pressure during an exacerbation of rheumatic fever in the case of A. L. W., a 13-year-old boy. Note the sharp rise in nitrogenous retention, which subsided. However, the rise in blood pressure persists to date without any urinary findings.

CASE 19.—A. L. W., a 13-year-old boy, was admitted to the Research and Educational Hospitals on April 27, 1944, complaining of general weakness and migrating joint pains. He was well until Christmas, 1943, when he developed a sore throat. One month before admission he had another sore throat, after which he became progressively listless, fatigued, and weak. A week prior to admission he had a severe pain in the right ankle; a day or two later the right knee and hip became involved. None of these pains were accompanied by erythema or swelling. There was also dyspnea on exertion for the previous two months.

Entrance.—The temperature was 100° F., pulse 130, respirations 28. Blood pressure was 130/80. Urine was negative for any abnormal elements on May 11 and 24, June 10 and 12, July 1 and 5. Lungs were clear; the pulmonary first sound was heard at the anterior

axillary line in the fourth interspace. There was a split first mitral sound, and a systolic murmur at the aortic area appeared to replace the first sound. The sedimentation rate was 28 mm. on entrance, 17 mm. on May 4, 9 mm. on May 24, and 24 mm. on June 16, 1944. Blood count showed a moderate anemia and a 4 per cent eosinophilia. On May 20 the standard urea clearance was 6 c.c., on May 24 a maximum urea clearance of 12 c.c., on June 8 a standard clearance was 22.4 c.c. per 100 c.c. of blood. The nonprotein nitrogen on April 28 was 36; it gradually rose to 137 on June 7 and dropped again to 35 on July 8. The urea nitrogen ran a parallel course reaching the peak of 109 on June 7 and dropping to 13 on July 8. This gave the amazing urea ratio of 80 on June 7. On x-ray examination the heart showed enlargement to the right and left.

A diagnosis of acute rheumatic fever with mitral and aortic stenosis was made. Most interesting was the rise in blood pressure from the admission figure of 130/80 on April 27 to 140/85 on May 10, 170/100 on May 26, 160/110 on May 31, 170/100 to 156/110 on June 8, 172/110 on June 15, 160/100 on July 6, and 144/90 on July 14. All this occurred simultaneously with the retention of nitrogen and no urinary findings, certainly no red cells to suggest a nephritis (Fig. 3).

On readmission, Sept. 5, 1944, hourly blood pressures varied from 160/110 to 136/88. The latter figure was obtained while asleep under sodium amytal. Urea clearance was 38 c.c. standard clearance. He left with a casual blood pressure (being up and around) of 170/98; there were still no red cells or albumin on repeated examinations, but during the second admission there were hyaline casts. Further study in the outpatient department revealed that the hypertension was limited to the upper extremities; both femorals were only faintly palpable. However, a typical picture of coarctation of the aorta could not be ascertained.

Comment.—On reviewing this case, it seemed that while at the hospital and during the course of the acute rheumatic fever, a vascular accident occurred, which seriously impaired the renal function and closed his aortic bifurcation. This could have been an embolic or thrombotic process, not unlike the one Scupham and one of us (G. de T.[15b]) reported in the presence of a diffuse lupus erythematosus.

The significance of this history lies in the fact that under our own eyes there developed a case of juvenile essential hypertension in the course of a rheumatic infection. We have advocated surgery for this lesion.

UNCLASSIFIED GROUP

It would obviously be desirable to place all our patients with hypertension in the neurogenic or one of the renal groups. However, in our present state of knowledge this does not always seem possible (Table I).

COMMENT

Two groups of workers, Gregory and Levin,[24] and Page and his group,[1] have attempted to use spinal anesthesia with the idea that neurogenic renal vasoconstriction would be abolished, but not the humoral type; if the patient's blood pressure fell markedly a neurogenic type of hypertension was postulated which seemed amenable to sympathectomy whereas the renal, humoral type would maintain the blood pressure and was not fit for surgery. Surgeons using high spinal anesthesia are aware of the fact that blood pressure may often fall to very low level, this being due to a failure of venous return and a poor cir-

culatory adjustment to a sudden demand for compensatory measures.* In Grimson's animal experiments,[25] low cervical cord section lowered the hypertension of all animals, whether it was produced by elimination of the buffer nerves or after a Goldblatt clamp was applied; this latter, renal hypertension, did not respond as well in such acute experiments, which are not easy to apply to chronic human hypertension. Our observations, on man, dating back many years, have convinced us that in the first place the differentiation of renal from neurogenic hypertension is often impossible; and that the neurogenic phase may well be followed by a renal arteriolosclerosis just as repeated attacks of vascular spasm in the digits will result in digital vascular occlusion in Raynaud's phenomena. Conversely, pressor substances originating from the kidney may sensitize the sympathetic-adrenal mechanism as would appear from Heinbecker's experiments.[26] Contrary to expectation, our best results have been obtained in patients in whom renal vascular damage was obvious, whereas the "neurogenic" or "neuroendocrine" type responded poorly. It should be stressed that nervous stimulation not only activates the adrenals and the peripheral vascular bed, but may also affect the hypothalamic pituitary mechanism. In this latter variety, which according to Griffith and co-workers[12] comprises about 5 per cent of all hypertensives, splanchnic nerve section is ineffective. The nervous stimulus mobilizes the posterior pituitary principle, vasopressin, which is identical with the antidiuretic hormone thus acting directly on both the kidney and the peripheral vascular bed.

What is badly needed is a simple clinical test to detect this principle in the blood and so separate this group of patients from the essential hypertensives. They could have pituitary radiation but surgically only section of the pituitary stalk could be effective. In one such human case, the blood pressure actually fell to normal and diabetes insipidus did not develop.[27] We certainly are not advocating this method except to indicate the futility of splanchnicectomy in such a case.

In another paper[3] it was stated that the juvenile patient with hypertension whose basal diastolic blood pressure (after rest, sleep, or sedatives) still exceeds 90 mm. of mercury is the ideal surgical case; that in a second group irreversible changes exist but symptomatic relief is obtained and progress toward a malignant phase may be averted; that the patient in a premalignant or malignant phase has not derived any benefit from splanchnic nerve section in our hands. The conclusions which the present series of observations justify are that the so-called neurogenic group has not responded too well to this operation, whereas the "renal" group, provided renal damage is not too advanced, has responded favorably. Patients with pyelonephritis, post toxemic hypertension, streptococcus nephritis, and rheumatic renovascular damage are favorable candidates when the original process has subsided and the resulting renal arteriolar sclerosis remains. There is a possibility that the so-called neurogenic hypertension

*In their latest experiments, Gregory and his associates (Arch. Int. Med. 77: 385, 1946) found that when spinal anesthesia lowered the blood pressure of hypertensives to normal, inulin and diodrast clearances fell; this is one more argument in our opinion (but not in the authors') that hypotension induced by spinal anesthesia is not the equivalent of the reduction of pressure following splanchnic nerve section.

while activated by the central nervous system is a pluriglandular type of hypertension governed by the pituitary. Such patients may not respond to splanchnic nerve section and a simple, clear-cut biologic test would be most welcome to separate them from the operable cases.

SUMMARY

A group of case histories is presented of hypertensive patients who have done well, moderately well, and poorly after splanchnic nerve section. The operation used was a transdiaphragmatic approach and technically left nothing to be desired. The clinical history and renal biopsies have allowed us to separate a group of patients who suffered organic renal damage and showed good response to surgery. On the other hand, the so-called neurogenic group failed to respond even though there was little or no detectable damage. The suggestion is made that such hypertension exhibits a hypothalamic-pituitary stimulation which is not mediated by the sympathetic nervous system.

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FASCIA LATA REGENERATION

Animal Experimentation

J. C. Foshee, M.D., Grand Rapids, Mich.

SINCE I had done explorations on the thigh of man for the purpose of observing the process of fascia lata repair in ten patients from whom I had removed fascia lata for various surgical reconstructive procedures,[1] it was now my desire to know certain facts pertaining to this regeneration, which could perhaps never be known except by animal experimentation. I desired to know why the regenerated fascia lata in man consisted of only two layers, whereas the original had three layers. It was my opinion that observation and biopsy of regeneration defects at various lengths of time from several days to a few weeks after it had been made would undoubtedly be of great value in determining this factor. Not only did I desire to determine the rate at which regenerated fascia formed, but also from whence it came, and how it developed.

This investigation began in October, 1944, and was completed in the summer of 1945. Twenty-two operative experiments were performed on three dogs at twelve different times. When two extremities were opened on one dog, as was the case occasionally at one setting, it was considered two experiments. In the few instances in which this was done, a different type of investigation and observation was carried out on each thigh.

At no time was the life of any dog endangered. In fact, not one dog was really ill during the nine months of this investigation. Preoperative sedation with morphine sulfate hypodermically, followed by open drop ether, was the routine anesthesia employed. There were no infected wounds. In two instances a hematoma developed beneath the skin flap which interfered with the desired observation. In each of these two instances the experiment was considered a loss. These two hematomas should not be a surprise when one considers the great redundancy of skin and superficial fascia present in the thigh of the dog. Besides, one cannot apply a pressure bandage to the thigh of a dog as one can in man. Fine silk sutures were used throughout in this work. Each dog weighed approximately thirty pounds. The operative field was prepared by clipping the hair of the thigh, and then shaving it clean. The skin was washed with soap and water, dried, and painted with 50 per cent tincture of iodine. Sterile technique was used in each operative procedure throughout. All wounds were closed with interrupted silk sutures taking the skin, subcutaneous fat, and superficial fascia in one layer.

EXPERIMENTS

Experiment 1.—Dog 2078, Oct. 11, 1944. The left thigh was opened down to the fascia lata by a vertical incision on the external surface at the junction of the middle and lower third. The fascia lata was cleaned off by pushing the

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superficial fat and fascia aside, and a piece of the fascia lata 2 cm. square was removed. Two small vessels were tied with fine silk for hemostasis, and the wound was closed in the usual way. Microscopic study of this specimen showed it to contain three layers identical to that of man, namely, an inner and outer transverse layer, and a middle longitudinal layer (Fig. 1).

Fig. 1.—Normal fascia lata, three layers.

EXPERIMENT 2.—Dog 2078, Dec. 6, 1944. The left thigh was reopened by excising the old skin scar to expose the defect made by the previous operation. The reparative process was so extensive and the superficial fascia so dense that it was impossible to ascertain the exact area from which fascia lata had been removed. After that the border of all defects from which fascia lata was removed was marked with fine black silk in order that they might be identified easily when explored again. A specimen was removed which was thought to include the regenerated fascia with a narrow rim of the normal surrounding fascia lata on all sides, but a microscopic study made of slides taken from this tissue proved inconclusive. However, the defect now was greater than ever, and offered hope for a future exploration with a more satisfactory histologic study of the regenerative material. Therefore, the margins were marked with fine black silk interrupted stitches to make identification easy at a subsequent exploration.

EXPERIMENT 3.—Dog 2078, Jan. 31, 1945. The left thigh was reopened by excising the old scar and deflecting the flaps on either side. For the first time two layers of superficial fascia were found in a dog, each of which had under-

gone hypertrophy from operative trauma. In this case both layers were cleanly dissected off the true fascia lata until the defect made by the previous operation and outlined by the black silk came into view plainly. There was a layer of grayish-white fascial membrane growing toward the center of the defect from the fascia lata margins on all sides. The membrane seemed to come from the normal fascia lata, and was in continuity with it. There was an area about 1 cm. in diameter in the middle of this defect which had not yet been filled in by this membrane of new fascia. This new membrane seemed of a lighter gray, more of the color of normal fascia lata toward the periphery of the defect, and darker in color toward the center. An incision was made through the normal fascia lata all the way around the defect about 1 cm. from the edge, and a block

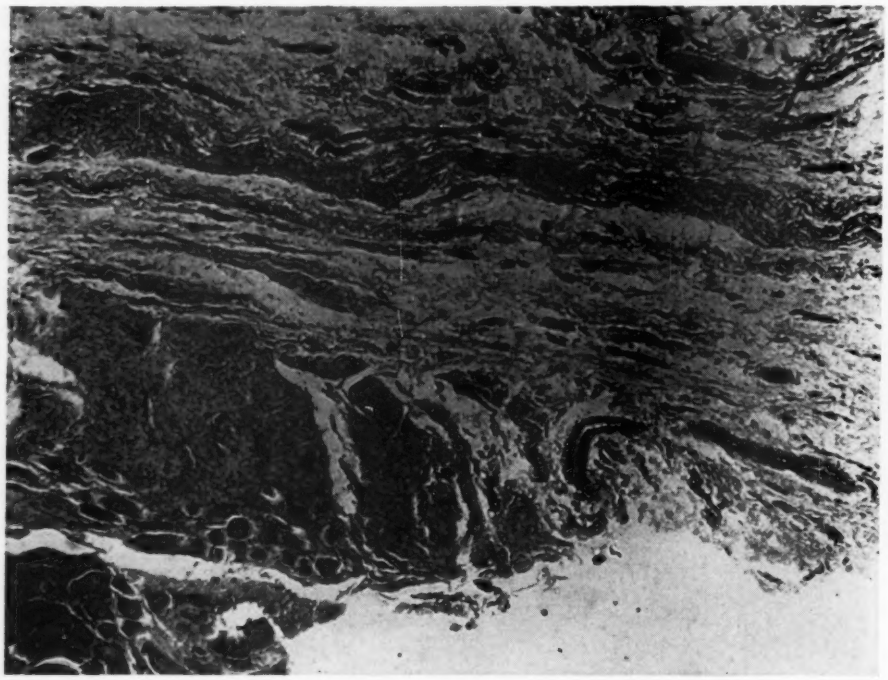

Fig. 2.—Regenerated fascia lata tapering off. Outer layer becomes thinner, inner layer stops in the lower right. Few muscle bundles in the lower left.

of tissue including this rim of normal fascia lata and the new regenerated fascia was dissected up from the muscle below. The edges of the normal fascia lata were a little more adherent to the muscle than normally, but the new regenerated fascia growing across the defect was not, and the new fascia became progressively thinner as it grew toward the center of the defect (Fig. 2). The margins of this defect, now larger than before, were marked by frequent interrupted stitches of fine black silk, and the skin and subcutaneous tissues were closed in the usual way.

Experiment 4.—Dog 2078, Jan. 31, 1945. The right thigh was opened for the first time. The fascia lata was exposed and a portion of fascia lata 3 cm. square from the lowest and strongest portion near the knee was removed. The

border of the defect was marked with continuous stitch of black silk, and the wound was closed in one layer of interrupted silk in the usual way.

EXPERIMENT 5.—Dog 2078, Feb. 21, 1945. The left thigh was again opened by excising the previous skin scar. Superficial fascia and subcutaneous tissues were dissected away to either side with moist gauze and scissors until the defect and its reparative process came into plain view. The regenerated fascia of the entire defect with 1 cm. of normal fascia lata all around the marked black silk was removed for study. The specimen grossly gave the impression that the regenerated fascia was coming from the margins of normal fascia lata on all sides. Toward the center it was of a grayish-red color, smooth, and tapered off, getting thinner at its inner edge near the center, and there was an area in the center 1½ cm. in diameter that was void of this membrane. The fibers of the red muscle showed very plainly in the center for they were not covered by the regenerated fascia. In Fig. 3 is shown, on the left half of the slide, the edge

Fig. 3.—Normal fascia lata with silk markers in left; regenerated fascia lata with only inner and outer layers continuing.

of two black silk markers in the margin of normal fascia lata containing three layers; whereas, in about the center of this view the middle layer terminated and the hypertrophied inner and outer layers fused to continue as one layer of regenerated fascia lata. According to Weller, the area in the left half in front of the silk and between the inner and outer layers proximal to their union was proliferating connective tissue looking more like regenerated fascia than ordinary scar tissue. This was undoubtedly a proliferation of the middle layer where the silk and trauma had partly destroyed it at its very margin.

EXPERIMENT 6.—Dog 2078, Feb. 21, 1945. The right thigh was reopened. The defect, which had been outlined with fine black silk sutures in the very lowest part of the fascia lata, was excised taking a very narrow margin of the normal fascia lata on all sides (Fig. 4). This left a rectangular defect about 3 cm. long with the long axis of the thigh and 3½ cm. wide transversely with the thigh. The fascia lata above this region was now freed of its overlying superficial fascia and subcutaneous fat for a good distance; another piece of fascia lata of identical size and shape was removed above the first defect, but leaving an undisturbed piece of fascia lata between the two defects 1½ cm. wide with the long axis of the high and 3½ cm. long transversely with the thigh. In other words, there was an intervening bridge of normal fascia lata across the lower third of the thigh, undisturbed, between the two defects. The edges of this

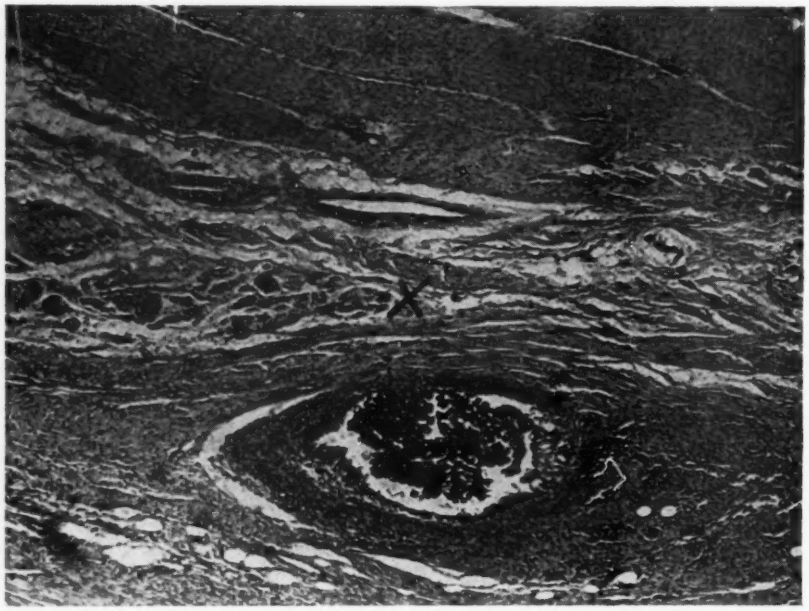

Fig. 4.—Left half, normal fascia lata margin; right half, regenerated fascia lata. Note middle layer terminates at point *X*, even with the black silk marker.

normal strip of intervening fascia lata were marked with a continuous suture of fine black silk. It was obvious that this would be of great help in the study of the regenerated fascia that should develop in these two defects since its direct relationship grossly and microscopically to the intervening strip of normal fascia lata could be accurately observed.

EXPERIMENT 7.—Dog 2078, April 11, 1945. The right thigh was reopened. The two defects and intervening strip of normal fascia lata, with its fine black silk thread clearly outlining its borders, was very vivid after the superficial fascia and fat had been cleanly dissected away. The two defects were filled in with a new layer of smooth fascia which was of the same color and apparent thickness as that of the normal fascia lata strip in between, as well as the normal

fascia lata all around. Both defects and all surrounding normal fascia lata were covered with one common thin external sheath. The whole would give one the impression that no fascia lata had ever been removed. But on palpation it could be felt that the intervening strip was probably just a little thicker. However, without the fine black silk markers it would have been impossible to distinguish the intervening strip of fascia lata from the regenerated fascia lata on each side.

The normal fascia lata was cut transversely across the thigh 2½ cm. proximal to the transverse normal strip and 2½ cm. distally. These transverse incisions extended into the normal fascia lata margins mesially and laterally for 1 cm., and their two ends were connected by two longitudinal incisions through the normal fascia lata margins 1 cm. from their edges. This block of tissue consisted of the regenerated fascia of the two previous defects and the intervening normal fascia as well as 1 cm. of fascia of the mesial and lateral margins enclosed in common internal and external sheaths. The slides (Fig. 5) show that the strong middle layer of longitudinal fibers do not regenerate nor extend themselves at all, but remain static at the silk thread markers on either side of the intervening strip of normal fascia lata, whereas the inner and outer layers of transverse fibers cut somewhat obliquely with their course do extend onward directly by continuity across the defect together as one dense layer of well-organized parallel fibers of fascia, and each layer undergoes hypertrophy to compensate in thickness and strength required in the absence of the middle layer.

EXPERIMENT 8.—Dog 2077, Oct. 11, 1944. An incision was made over the lower anterolateral surface of the lower third of the left thigh. The fascia lata was exposed and a piece 2½ cm. square was taken up, turned one quarter around, turned over so that the outer surface became the inner surface, and resutured in position with fine black silk. The skin was closed in the usual way.

EXPERIMENT 9.—Dog 2077, Jan. 17, 1945. The block of fascia sutured down with silk in Experiment 8 together with 1 cm. of the normal fascia around it was removed. The replaced block was exactly the same thickness as that of the surrounding fascia, and the inner and outer sheaths were in continuity. Only by the fine knots of black silk could the area be outlined. The specimen (Fig. 6) was cut transversely to the long axis of the middle longitudinal fibers on the margin as seen in the left one-third of the specimen, and parallel to the middle longitudinal fibers in the block that was turned one quarter around as noted in the distal two-thirds of the slide. The line of union between the block and the margin may be seen directly between the two silk sutures. The middle longitudinal layer was thicker to the left of this line of union than to the right, and the inner and outer transverse layers were thicker and better developed to the right than to the left of the silk threads and this line of union. This did not show as distinctly in this one field as it did when studied under the microscope with a view of a larger area, in which it was very obvious. This confirms the work of Kleinschmidt.[2] That is, when the longitudinal fibers were

Fig. 5.—Between the two black silk markers are the three layers of the intervening strip of normal fascia lata. On each side, right and left, there is a total absence of the middle layer in the two areas of regenerated fascia lata, but the inner and outer layers have extended across both defects in continuity from their respective layers of the normal fascia lata.

placed so that they did not take up the pull that was usually required of them they became thinner; whereas, the inner and outer transverse layers became thicker and better developed from taking on the pull which the middle longitudinal fibers previously maintained. Some of the inner and outer layers of transverse fibers were outside of the silk suture on either side, whereas all the middle longitudinal fibers were seen plainly in the middle with a good amount of the inner and outer transverse fibers running between the middle fibers and the silk sutures.

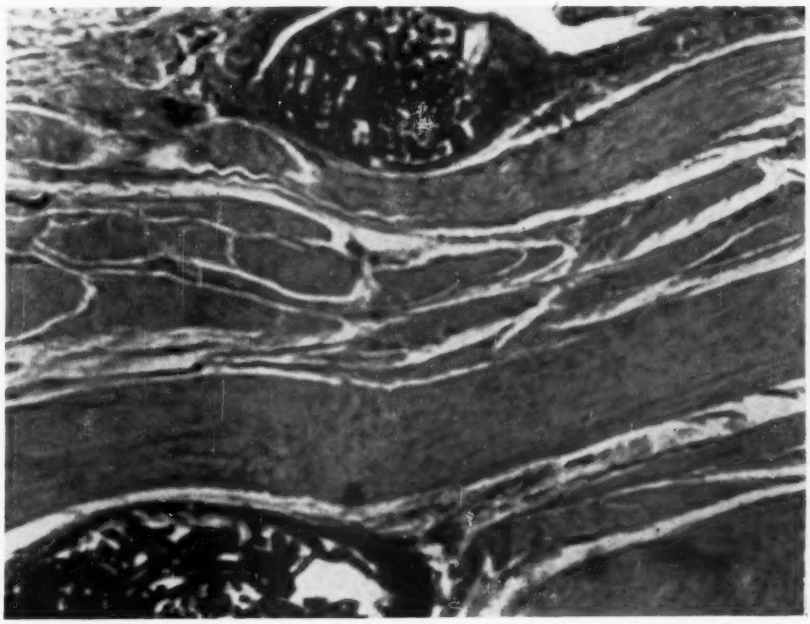

Fig. 6.—Flattened and atrophied middle layer of bundles to the right of silk with hypertrophy of the inner and outer layers.

EXPERIMENT 10.—Dog 2077, Jan. 31, 1945. The left thigh was reopened by making an incision around the old scar and taking a block of elliptically shaped tissue down through the fascia lata. A study of the tissue revealed the identical layers found in the normal thigh; the skin, subcutaneous fat, two layers of superficial fascia, a thin layer of adipose or areolar tissue and the fascia lata. The fascia lata defect with its regenerated fascia was in the bottom of this block. A study of this defect made by removal of the block of fascia lata in Experiment 9 showed that it had half filled in with a new, thin, slightly reddish layer of fascia lata extending from the margins, and it was covered with a thin sheath which was in continuity with the sheath of surrounding fascia lata. The muscle fibers beneath were faintly visible because of the thinness of the new regenerated fascia which was somewhat transparent. The center of this defect for an area of 2 cm. square was not filled in with regenerated fascia and the muscle was bare. This regenerated material was removed along one side with silk sutures, which were placed two weeks before for identification,

Fig. 7.—Three layers of normal fascia lata of left third. Two layers of regenerated fascia lata in right two-thirds. Common external sheath above.

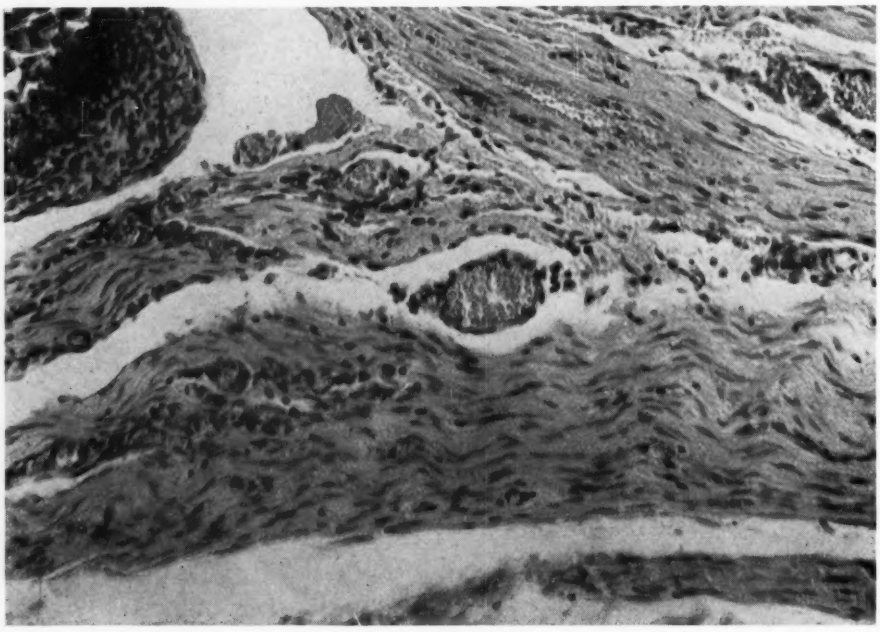

Fig. 8.—Left upper corner, black silk marker on margin of defect. To the right, internal and external layers fuse and continue on in orderly fashion to form the regenerated fascia lata. Common internal sheath below.

together with a little of the margin of normal fascia lata. A slide (Fig. 7) made from this tissue shows the margin with the three usual layers in the left third of the slide and the new regenerated fascia just forming, fourteen days old, occupying the right two-thirds. It is interesting to note that the internal layer was extending on independently of the external layer from which it was separated by adipose tissue, and it was fully twice as thick and as well developed as the external layer. Some of the fibers of the internal and external layers have united just in front of the termination of the middle layer.

EXPERIMENT 11.—Dog 2077, Feb. 21, 1945. Again the left thigh was reopened to observe the defect made three weeks before, and it was found that the regenerated fascia lata had spread almost all over the thigh defect. There was an area 1 cm. wide in the middle which was not covered with the regenerated fascia. The muscle fibers here were bare. The regenerated fascia defect and a little of the normal fascia lata margin was removed. A slide made from the margin is shown in Fig. 8. Before the incision in the leg was closed the margins of this very large defect which was about four inches square were marked with continuous black silk suture for further identity.

EXPERIMENT 12.—Dog 2077, April 11, 1945. Following this experiment a large hematoma developed in the wound, which was evacuated. An interrupted suture or two was removed in the middle of the wound. After some clots were expressed the wound healed quite readily, but it was feared that any future value from opening the thigh would be lost. However, to make certain, the thigh was opened and it was found that superficial fascia proliferation and edema so obscured the field that the experiment had to be considered a loss. The wound was closed by primary suture and a temporary pressure bandage applied.

EXPERIMENT 13.—Dog 2077, April 11, 1945. The right thigh was opened for the first time and Experiment 7 of Dog 2078 was repeated. A wide area of the fascia lata was freed of its superficial fat. Two blocks of tissue 3 cm. square were removed, leaving an intervening piece of undisturbed fascia lata between the two defects 1½ cm. wide. The two edges of the intervening piece of normal fascia lata were marked with a very fine continuous black silk suture, and the skin was closed.

EXPERIMENT 14.—Dog 2077, May 9, 1945. The right thigh was reopened by an elliptical incision around the old scar. After the skin and subcutaneous fat had been incised and brushed aside with moist gauze, a well-defined layer of superficial fascia came into view. It was dissected off and then another layer of superficial fascia appeared which was thicker than the first. It was dissected off. With moist gauze, a little fat and areolar tissue were brushed away to expose the regenerated fascia lata immediately beneath with the intervening strip of normal fascia lata well outlined with the black silk suture. Grossly the appearance of the normal fascia lata between, at each end, and at the sides of the defects seemed of the same thickness, color, and consistency as the regenerated fascia of the defects. Were it not for the black silk sutures it would have been

Fig. 9.—In placing the silk a deep bite was taken so that the termination of the middle layer which is the very margin of the intervening strip of normal fascia lata is just outside the black silk sutures. The inner and outer layers, only, continue onward to the right and left to form regenerated fascia lata.

impossible to identify the defect. The external sheath of the normal fascia lata continued over the defect and was in direct continuity without any scar tissue or contracture whatsoever. The regenerated fascia lata of the defects and the intervening normal fascia lata strip were removed en masse. When they were stripped away from the underlying muscles, it was striking to note the fact that they all appeared as one single piece of fascia covered by a common internal and a common external sheath, which extended across from the normal fascia lata. No one part of the block was any more adherent to the underlying muscles than the other. In fact, it was all in loose approximation as was the normal fascia lata elsewhere. Several blocks of tissue were taken in this specimen for histologic study. The most interesting block perhaps is the one taken through the middle of the intervening strip of normal fascia lata and extending on into each defect to the right and to the left, each for 1 cm. (Fig. 9). Under high magnification the silk sutures appeared to be a little inside the outer edge of the middle longitudinal fibers. Of course, this was a continuous stitch and it was placed a little inside in order that it would be secure. But it showed very definitely that the well-outlined middle longitudinal layer shown in bundles had not regenerated either to the right or to the left, but the inner and outer transverse layers have extended onward in direct continuity without a wave or hesitation to form the regenerated fascia lata; their formation when the whole slide was studied in many different fields showed that their thickness had compensated for the absence of the middle layer in maintaining the strength and function of the normal fascia lata. This accounts for there being no depression or thinning out of the fascia at the site of the defects as shown by gross and microscopic examination. The same thing was true in Experiment 7. In other words, the inner and outer layers seem actually to be hypertrophied as they cross the defects.

EXPERIMENT 15.—Dog 2079, Oct. 11, 1944. The left thigh was opened to expose the fascia lata in the lower third of the outer surface. A piece of fascia lata 2 cm. square was removed, turned one quarter around, but not turned over, and sutured into place with interrupted fine black silk. Above this area another small piece of fascia lata was taken for a study of the normal fascia lata of this dog (Fig. 10), and it shows the normal three layers of fascia lata.

EXPERIMENT 16.—Dog 2079, Jan. 17, 1945. A block of fascia lata containing the block sutured into place with the margin of the normal undisturbed fascia lata on the four sides was removed en bloc, containing the fine silk knots which identified the quarter-turned block of fascia. The edges of this larger defect were marked with fine black silk sutures for future identity. A section made for study through the margin of the normal undisturbed fascia lata and the graft (Fig. 11) shows in the left fourth the middle longitudinal layer, cut obliquely and nearly parallel to its fibers, to be thicker and stronger than either of the outer layers as would be expected in the undisturbed margin. Whereas in the right half, which is the graft turned quarter around, the middle layer which is now a transverse layer was not as dense as the hypertrophied internal

layer, and about as dense as the outer layer. The inner and outer layers have taken on the pull formerly performed by the middle layer. *X* to *Y* is the line of union of the graft and the undisturbed fascia lata margin. This further verifies the findings of Kleinschmidt[2] and Experiment 9 of this article.

EXPERIMENT 17.—Dog 2079, Feb. 21, 1945. The left leg was reopened to inspect this large defect and a beautiful specimen was observed showing the normal margins of fascia lata marked out with interrupted black silk previously placed, and a new fascia lata one-half as thick as the normal going completely across the defect. The external sheath of the normal fascia lata was in continuity cross the new fascia lata. In the left two-thirds can be noticed the three layers of normal fascia lata with the middle layer terminating, and in the outer third the inner and outer layers of transverse fibers, only, continue on to form the new thin regenerated fascia (Fig. 12). The defect was again marked with silk and the skin closed.

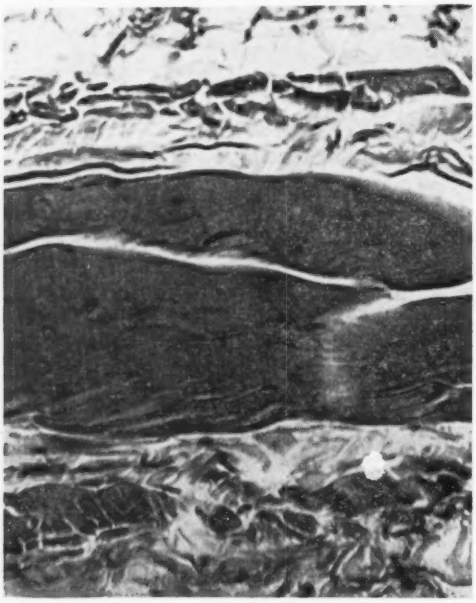

Fig. 10.—Normal fascia lata, three layers.

EXPERIMENT 18.—Dog 2079, Feb. 21, 1945. The right thigh was opened for the first time and a piece of fascia lata 4 cm. square was removed. The edges of the defect were marked with an interrupted layer of fine black silk. High magnification of this area (Fig. 13) shows the three layers in normal fascia lata.

EXPERIMENT 19.—Dog 2079, March 9, 1945. The left leg was reopened, and the large defect heretofore outlined with fine black silk was inspected. It was contracted a bit, being only about two-thirds the size expected, and it was filled in with a thin layer of regenerated fascia lata. In the center it was so thin

that the muscle beneath could be visualized, but on its periphery it was too well formed for that, and the whole was covered with a sheath from the normal fascia lata which came across in continuity. A section (Fig. 14) shows a picture similar to that shown in Experiment 17. The middle layer terminated in the left third and the inner and outer layers extended across to form the new fascia.

EXPERIMENT 20.—Dog 2079, March 9, 1945. The right thigh was reopened, the defect observed, and in this instance the superficial fascia had dipped down

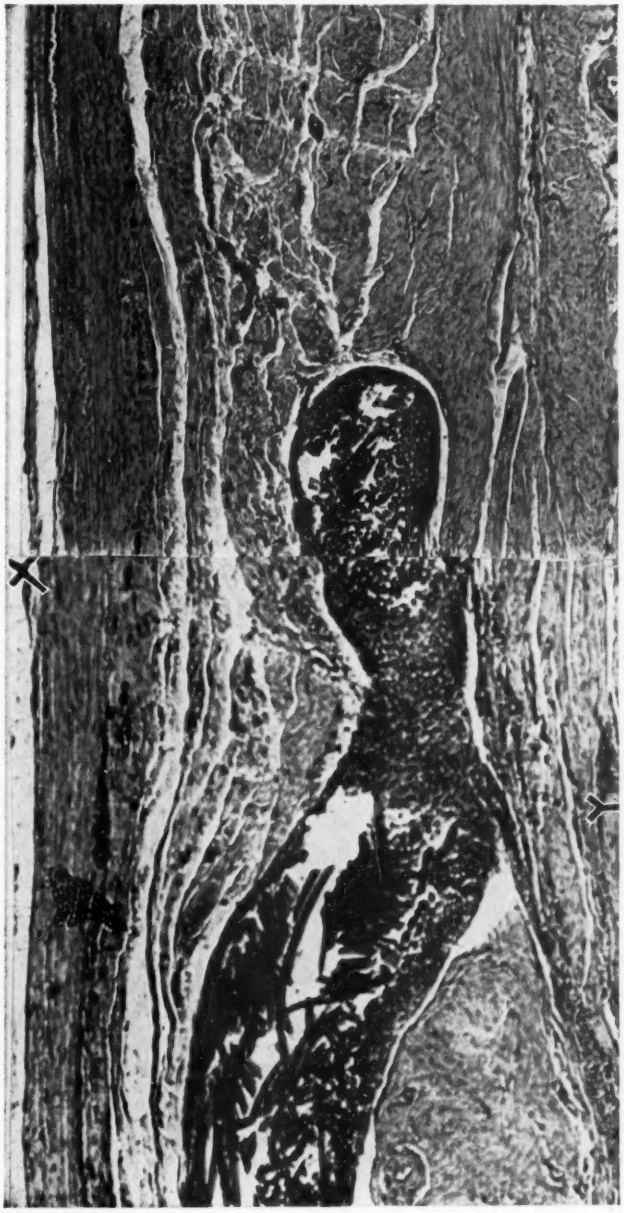

Fig. 11.—Left third is normal margin with thick middle layer and thinner inner and outer layers. Right half is the graft with the thicker inner and outer layers and thinner middle layer.

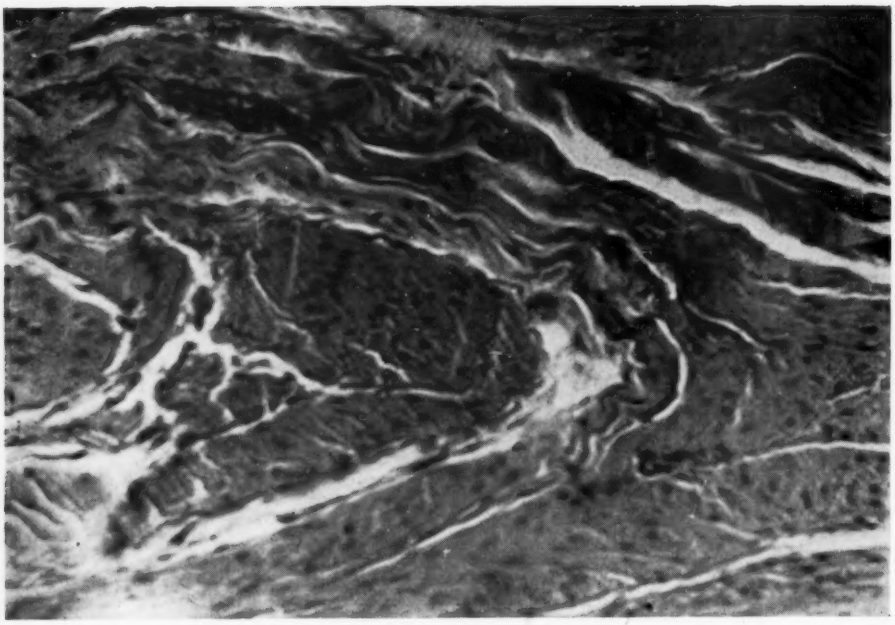

Fig. 12.—Left two-thirds shows three layers of normal fascia lata. Right one-third shows two layers of regenerated fascia lata.

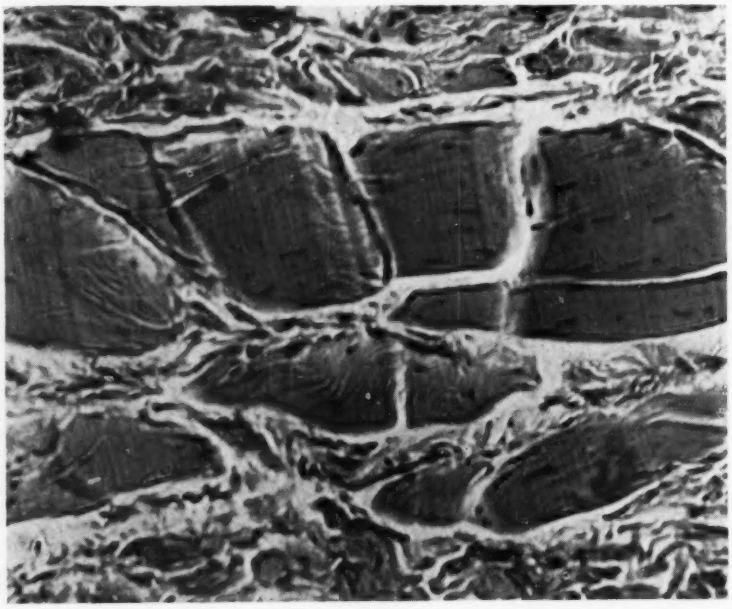

Fig. 13.—Strong middle longitudinal layers cut transversely. Inner and outer transverse layers cut parallel or somewhat obliquely.

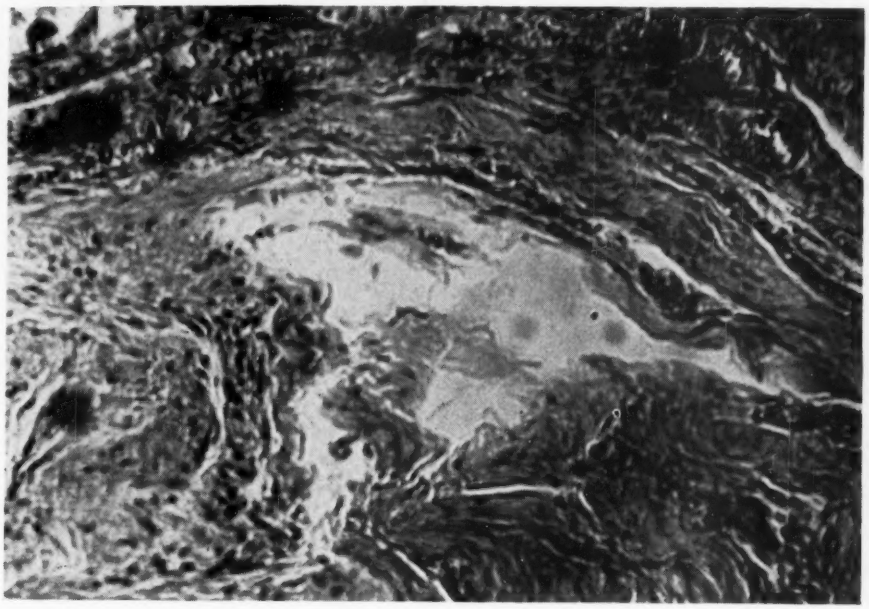

Fig. 14.—Three layers of normal fascia lata in left third, with inner and outer layers extending across in continuity.

Fig. 15.—Confusion of various layers.

into the defect to form scar tissue, the first that had been observed. It was rather difficult to dissect the superficial fascia off the defect. The superficial fascia had undergone so much hypertrophy and hyperplasia that it was as thick as one would expect fascia lata to be, but not as well outlined. After it was finally dissected away, the normal fascia layer with the black silk below was visible, but the defect had contracted and a large block was removed containing the silk in the hope that a section running from the margin of the normal fascia lata to the regenerated material in the defect might be found. The defect was again marked with fine black silk sutures. Microscopic study of this section (Fig. 15) shows a confusion of the various layers. At the top can be noted the sheath and a few parallel fibers of the external layer which ran across to the right and left of the black silk in continuity. Immediately beneath were some bundles of the middle layer to the right of the silk, and from there on downward below the level of the silk there was a mixture of layers, and marked hypertrophy of the inner layer. In the left lower center there were a few transverse fibers which were surrounded by fibers of the internal layer. In the right lower corner was the thickened sheath of the internal layer. This was an irregular pattern, and the only one so far observed.

EXPERIMENT 21.—Dog 2079, April 11, 1945. Thirty-three days later the right leg was reopened. Both layers of the superficial fascia were dissected off, each separately. The deeper layer was attached to the fascia lata with long trabeculations through an intervening layer of areolar tissue. When that was brushed away with a moist sponge the silk pattern, which outlined the defect, was found in the fascia lata below. A specimen 5 cm. square including normal fascia lata in the left half and the regenerated fascia in the right was taken for study. The silk stitches were in the middle of this specimen. A continuous silk suture was placed around the margin of the defect for future identification. A section was taken at the junction of the normal and the regenerated fascia lata. Microscopic study of a slide from this area (Fig. 16) shows the three layers of the normal fascia lata to the left of the silk and only two layers to the right, namely, the inner and outer layers which had extended across in continuity. The middle layer had not regenerated and stopped abruptly at the site of the silk marker.

EXPERIMENT 22.—Dog 2079, June 9, 1945. The wound was reopened and a suture of black silk was observed around the previous defect. A new layer of regenerated fascia lata extended across the defect. Microscopic study of a slide made from this area shows the termination of the middle longitudinal layer to the left and at the site of the black silk (Fig. 17); whereas, the inner and outer layers continue on and merge into one to form the thick regenerated fascia lata across the defect. The well-organized internal layer of parallel fibers which was more dense than the external layer extended across in continuity to make a thick substantial layer. Both layers combined made a firm layer of regenerated fascia lata enclosed within a common external sheath shown at the very top and a common internal sheath, which was not shown in this field.

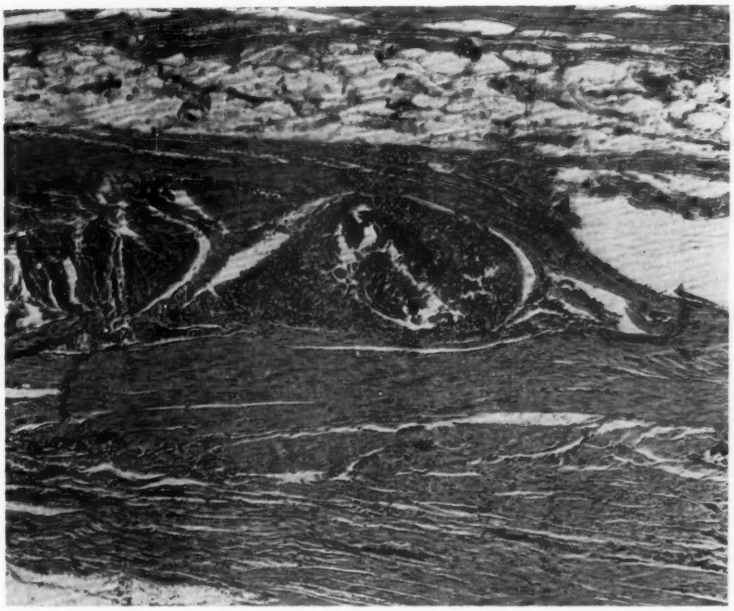

Fig. 16.—Middle layer stops left of silk; inner and outer layers continue on.

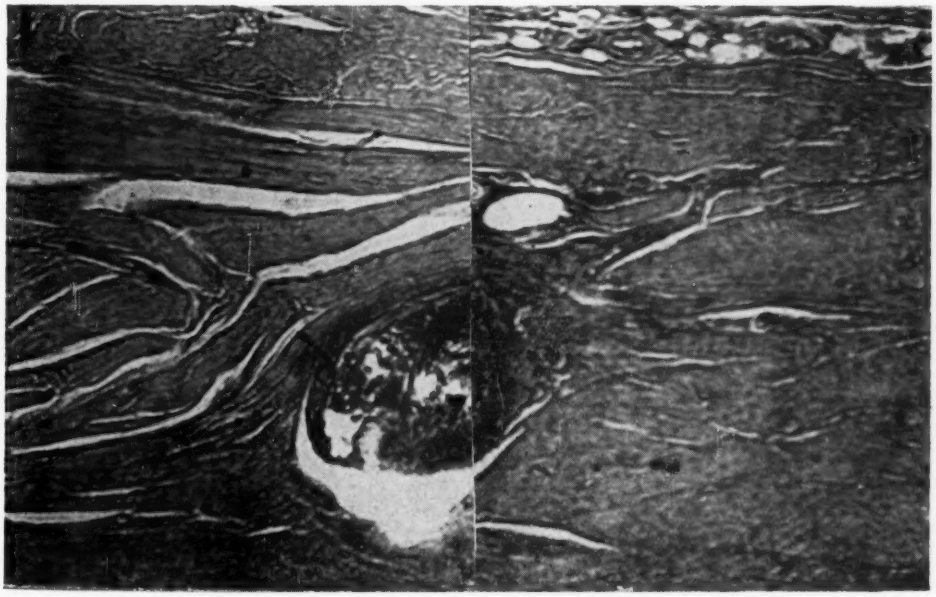

Fig. 17.—Three layers at the left of silk; two layers, inner and outer, continue on to the right of silk.

COMMENTS

The use of living fascia lata in reconstructive surgery is continually becoming of greater interest and importance. For many years large fascia lata grafts have been used in arthroplasty of the large joints. Not long ago Singleton and Stehouwer[3] reported the use of large fascia lata grafts in the repair of inguinal hernias. More recently Wangensteen[4] has used practically all the fascia lata as a pedicle flap to fill in the defect in the repair of large abdominal incisional hernias. No effort was made by the authors, or anyone I know, to attempt to reconstruct a fascial covering for the muscles of the thigh from which these large fascia grafts were removed. Such a repair would be impossible anyway. It is important to know what happens to a defect produced in fascia lata.

CONCLUSIONS

1. Twenty-two experiments on the fascia lata of dogs are reported. Regenerated fascia lata has been studied at various phases and stages from the fourteenth to the ninety-seventh day of its formation.

2. The inner and outer transverse layers regenerate by extension directly from their respective layers of the adjacent normal fascia lata together with their sheaths and blood vessels. The middle longitudinal layer does not regenerate.

3. In a medium-sized defect the average rate of regeneration is as follows: At the end of two weeks the regenerated fascia lata is only a thin veil. It becomes more dense rapidly. At three weeks it is a well-defined membrane. At one month it is half as thick as normal fascia lata, and at two months it is grossly and microscopically as thick as normal fascia lata. In a very large defect the process of regeneration may be slower, but in a smaller defect it may be so rapid that the regenerated fascia lata in one month will become as thick as the normal fascia lata.

4. Since the middle layer is always absent in the regenerated fascia lata, the inner and outer layers undergo hypertrophy and hyperplasia to compensate for the absence of the middle layer.

The author wishes to express his sincere appreciation to Dr. Frederick A. Coller, Chairman and Professor of the Department of Surgery of the University of Mcihigan at Ann Arbor, for the use of the laboratory of Experimental Surgery of the University and all of its facilities; and to Dr. C. V. Weller, Chairman and Professor of the Department of Pathology of the University for the histologic studies which he made in this research, and to Mr. W. J. Troy, Attendant in charge of the Experimental Laboratory, profound gratitude is expressed for his able assistance in that he administered the anesthesia in every experiment and cared for the animals nine months without an accident.

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FASCIA LATA REGENERATION

Final Report

J. C. Foshee, M.D., Grand Rapids, Mich.
(From the Department of Surgery, Butterworth Hospital)

THERE is a certain curiosity and inquisitive attitude in one's mind toward the reparative processes that take place when a structure so large and so important as fascia lata is removed in part or in whole. In my preliminary report upon the subject two years ago[1] I presented the first evidence that has appeared in the literature that fascia lata when removed from man does regenerate completely enough to be used again in surgical procedure should the demand for its use so arise. At that time five cases of regeneration were reported which I had personally observed. Since that publication, observations have been made by other surgeons in one or more cases that similar regeneration occurred, but no histologic studies were made. Coller[2] observed regeneration of fascia lata following a Kondoleon operation for elephantiasis of the lower extremity including the thigh in which the fascia lata had been removed in its entirety. The patient returned with a recurrence of elephantiasis and was re-operated upon. A large piece of new substantial fascia was removed from the thigh at the second operation, which looked like fascia lata to Coller, and he mentioned my work at that time to his associate who performed the operation. But, unfortunately, that specimen of fascia was lost at the University Hospital so that I was unable to obtain a specimen of it for study.

Such regeneration has also been observed by Smith[3] in a case in which he reopened a thigh to obtain more fascia lata in a procedure of plastic surgery. Singleton and Stehouwer[4] stated that they had observed the regeneration of fascia lata, but that they did not make biopsy or histologic studies of the regenerated material. They took it to be scar tissue. It is unfortunate that none of these surgeons made a histologic study of the regenerated fascia for, as I have shown and will show, it is not scar tissue but quite to the contrary it is a structure of well-organized layers of certain parts of the normal fascia lata, such layers having their own sheaths and these sheaths combined in a common sheath, each sheath with its own minute blood vessels as Kleinschmidt[5] and I[1] have heretofore shown.

When opening the thigh in an occasional case in which the subcutaneous fat and superficial fascia does not peel off the regenerated fascia so readily, one might form the opinion that he is dealing with a layer of scar tissue. I have observed one such case, but this is by far the exception rather than the rule, and when in such a case the regenerated fascia is dissected off the underlying muscles it becomes very evident that one is dealing with a real sheath of substantial fascia that is loosely attached to the muscles by thin trabeculations exactly as is normal fascia lata. When this layer of material is subjected to

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careful histologic studies, it will show definite regenerated layers of fascia lata always following a certain pattern as I have found repeatedly and reported previously.

In my preliminary report it was shown that normal fascia lata is comprised of three layers, namely, an inner transverse layer, an outer transverse layer, and a stronger middle longitudinal layer; that each layer is enclosed in its own fine sheath; and all three layers are enclosed in a denser common sheath. Certain proofs were presented that it was the inner and outer transverse layers that regenerated.

As further proof, five additional personal cases of regenerated fascia lata have been studied. Knowledge has been gathered from these cases which, it is hoped, will show conclusively the exact nature of the regeneration and other facts of value concerning the new fascia which forms.

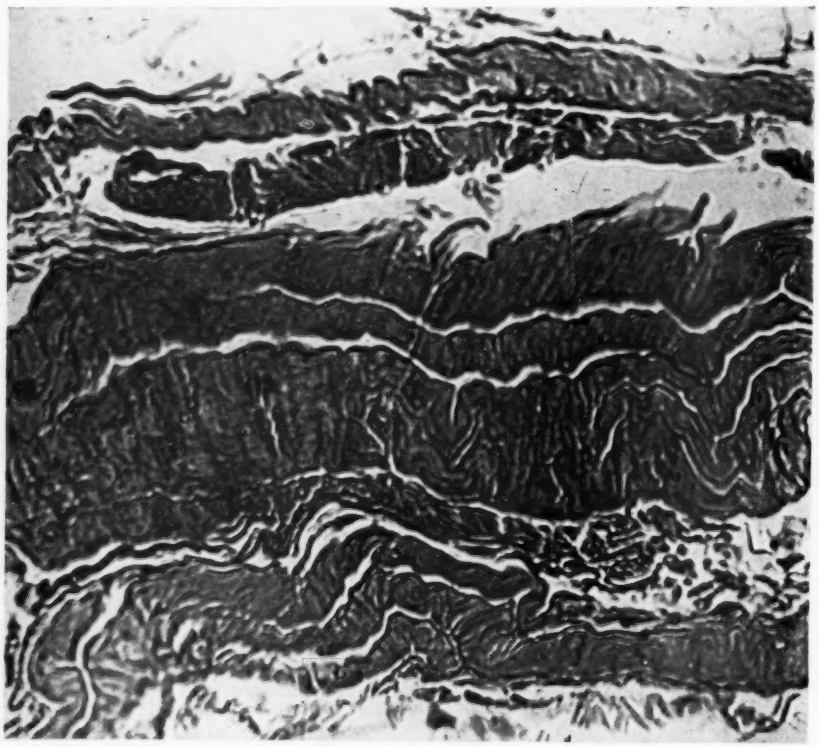

Fig. 14.—Normal fascia lata with outer transverse layer, middle longitudinal layer, and inner transverse layer. Each layer enclosed in a thin delicate sheath.

CASE REPORTS

CASE 1.—Mrs. P., aged 51 years, upon whom was performed an abdominal total panhysterectomy, May, 1938, for carcinoma of the fundus of the uterus, and whose immediate recovery was uneventful, returned two years later with an incisional hernia. At the time of operation she was quite obese and the obesity had increased markedly. She was a schoolteacher, who could ill afford to have the hernia repaired except during the summer vacation. During the following summer when she needed further recuperation, and there was uncer-

tainty of the ultimate success of the irradication of all the cancer, operation was discouraged, but in the summer of 1942 when she was apparently enjoying good health she insisted that the hernia, which was becoming larger and more troublesome all the time, be cured by surgical repair. Since it has for many years been my custom to repair nearly all ventral and incisional hernias with fascia lata, on July 23, 1942, the hernia was repaired, using among other material for suturing two pieces of fascia lata each one-half inch wide, and seven inches long, taken from the right thigh. About one year later, June 29, 1943, she permitted reopening of the right thigh to inspect the process of regeneration. It was found that the old fascia margins had spread apart for a distance of two inches and the area between had filled in with a smooth layer of fascia not quite as thick as the normal fascia lata margins but of the same color, and not more adherent to the overlying superficial fascia and underlying muscles than was the normal fascia lata. A specimen three inches square in the center was taken, which included the full width of the regenerated fascia lata and one-half inch of the medial and external margins of the old fascia. Grossly the inner and outer layers of regenerated fascia appeared in continuity with the corresponding inner and outer layers of the margins of fascia lata on both borders of the specimen, but the middle longitudinal layer of white fibers was not apparent in the regenerated part. In Fig. 1*A* are shown very clearly the three distinct

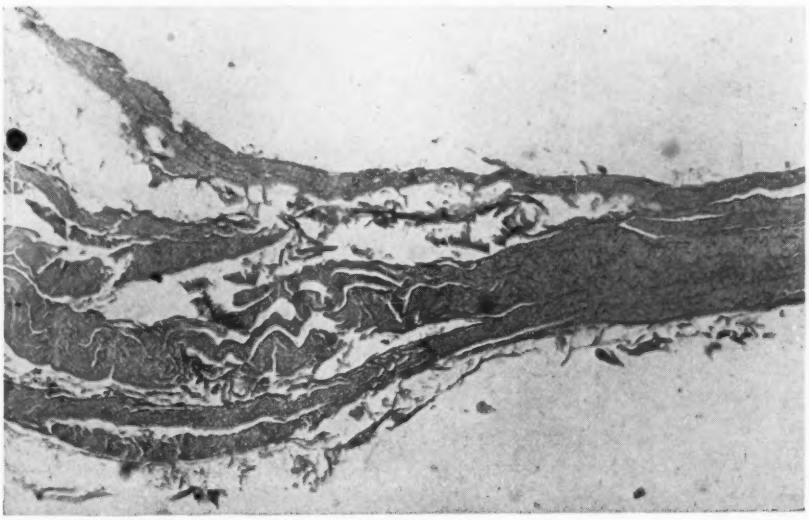

Fig. 1*B*.—Three layers of normal fascia lata on the left; two layers of regenerated fascia lata on the right.

layers in the normal fascia lata margin of the specimen cut a little obliquely instead of exactly transversely as intended. This cannot always be avoided. The inner and outer layers combined were about as thick as the middle layer. In Fig. 1*B*, a little further along in the specimen at another site at the end of the normal fascia margin and the beginning of the regenerated fascia, are shown the playing out and termination of the middle layer of fibers with the inner and outer layers extending across in continuity. They each became more dense as they fused together to form a thick layer of regenerated fascia.

CASE 2.—Mr. T., aged 52 years, on Oct. 30, 1928, had two strips of fascia lata taken from the right thigh and used for the repair of an incisional hernia in the upper right abdominal wall, which had followed a right paramesial incision for an operation for gastroenterostomy for the cure of a chronic stenosing duodenal ulcer in 1927. On Jan. 22, 1942, this patient submitted to operation for a recurrent direct inguinal hernia operated upon at first three years before, elsewhere. Fascia lata sutures were again removed from the right thigh of the patient for the repair of the hernia. This patient was a very large, obese man,

a heavy beer drinker, who lived an easy life and seldom used the skeletal muscles. In such a case we may expect to find very thin fascia everywhere in the body, hence a thin regenerated fascia. Exactly that was found. The medial margins of the fascia lata defect created by the removal of the fascia strips fifteen years before had retracted to the midline anteriorly and the external margins had retracted four inches laterally and posteriorly. There was just

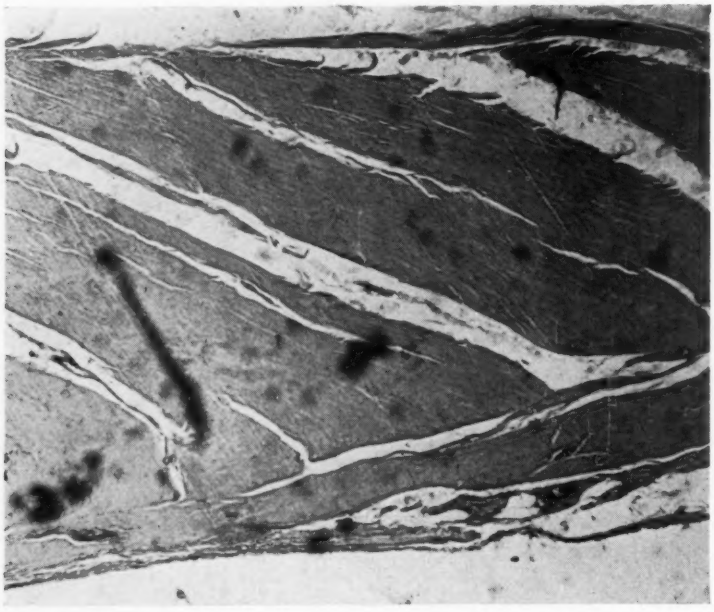

Fig. 2*A*.—Very thin outer layer; an inner layer three times as thick, and a very dense middle layer.

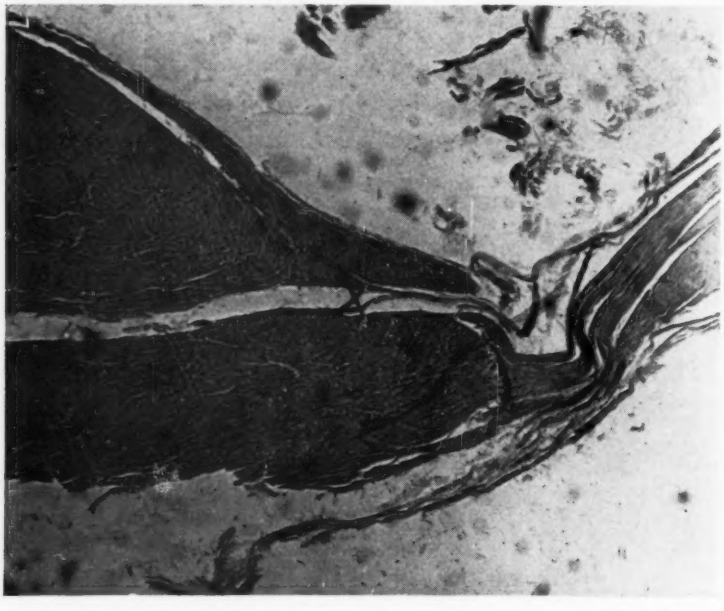

Fig. 2*B*.—Normal fascia lata margin of left two-thirds; regenerated right one-third.

enough of the old fascia lata left of the external shelf to make three strips three-eighths of an inch wide for the repair of this hernia. The intervening wide defect made fifteen years before was filled in with the thinnest of regenerated fascia lata which had been observed so far. A specimen of it was incised, taking a little of the medial border of the old fascia lata attached. In Fig. 2*A* are shown the three layers of the normal fascia border, and in Fig. 2*B* just one field further on in its very center the middle layer of fibers comes to a blunt ending. An attempt was made to cut this specimen transversely with the long axis of the thigh, but it was cut somewhat obliquely. The wide inner transverse layer of fibers goes on into the regenerated material after forming the curl and kink seen in the right half of the field. The outer transverse layer in this case was almost insignificant, being about one-fifth as thick as the inner layer and only its sheath and a few of its fibers were seen to continue with the internal layer to form the regenerated fascia to the right. In Fig. 2*C* is shown how the external layer farther in the regenerated fascia has faded out completely. The chief structure of the regenerated fascia was the inner transverse layer of the normal fascia lata. This accounted for this regenerated fascia being thinner than usual.

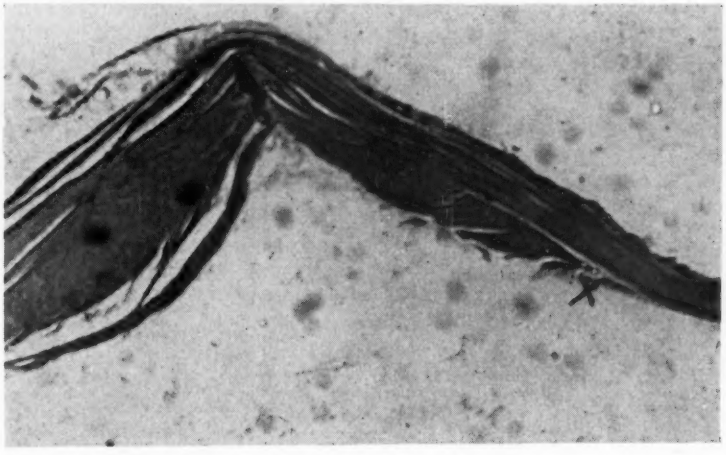

Fig. 2*C*.—Continuation of thin regenerated fascia; inner layer thins out at *X*.

Case 3.—Mr. S., aged 58 years, came on the surgical service March, 1941, with an acute exacerbation of a chronic intractable ulcerative colitis. He was in a critical condition and became worse every day in spite of all medical measures. After ample preparation an ileostomy was performed. The patient was so well afterward and so content that he refused colectomy although he occasionally had some mild residual recurrent symptoms. On Sept. 5, 1942, it was necessary to operate on him as an emergency for a strangulation of intestine in an incisional hernia below the ileostomy. He was an obese and inactive man. The use of living fascia lata sutures was deemed advisable, and three strips each three-eighths inch wide and seven inches long were removed from the right thigh for the repair. A cure of the hernia resulted. On Aug. 23, 1943, or about one year later, he kindly consented to have the thigh reopened for the purpose of studying and taking biopsy of the regenerated fascia lata. He was the only patient that had been seen who had a hernia of the vastus muscle one year after fascia lata had been removed, but it was confined strictly to the upper half of the incision in the thigh. Obviously it would be interesting to discover the reason for this unusual phenomenon. Under local anesthesia the old incision was opened. The superficial structures were carefully dissected off the regenerated fascia that filled the defect. While dissecting up the superficial fascia, fat, and skin in one layer from the regenerated fascia beneath, much to my surprise, the reason for the herniation was revealed. In the lower half of the defect a new well-developed regenerated fascia lata had formed, whereas in the upper half the

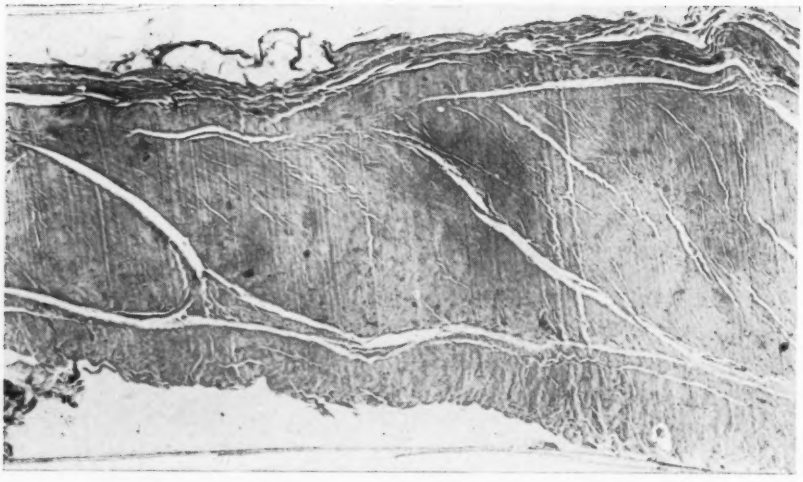

Fig. 3*A*.—Outer transverse, middle longitudinal, and inner transverse layers.

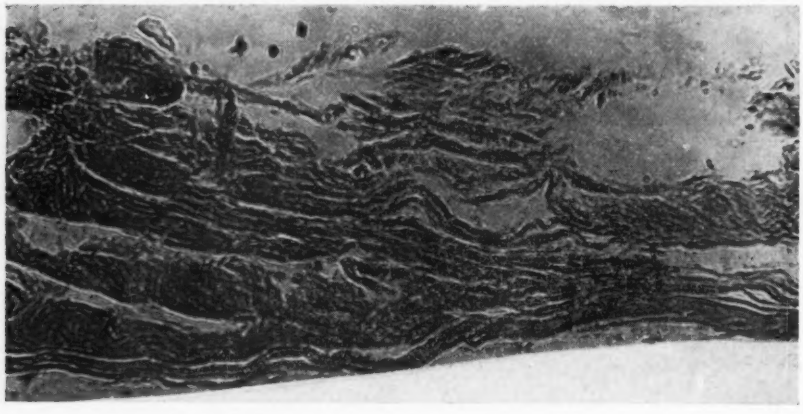

Fig. 3*B*.—Middle layer stops at *X*; inner and outer layers continue as the regenerated fascia.

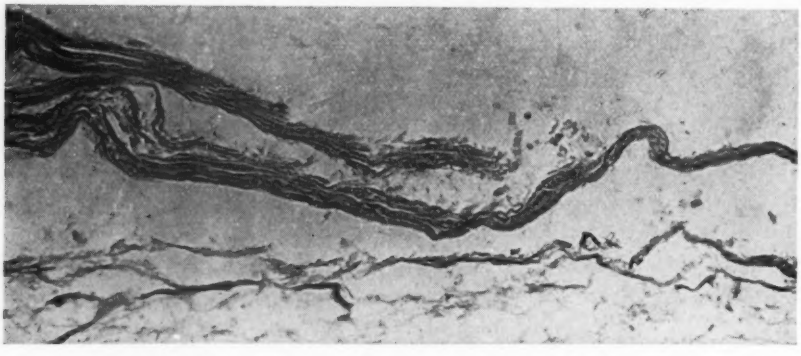

Fig. 3*C*.—Inner layer stops, outer goes on tapering off.

defect was filled in only by crisscross fibers of fibrous tissue which formed a coarse network structure from one of the old normal fascia margins to the other. In Fig. 3*A* is shown a cross section of a piece of normal fascia lata which was taken for histologic study at the time that the fascia lata sutures were removed for the hernial repair. The weakness of the normal fascia was evident. The outer transverse layer was so thin it was of little use. The inner transverse layer was twice as thick as the outer layer, but less than one-third as thick as the middle layer. In Fig. 3*B* are shown a termination of the middle layer of fibers at the fascia margin (*X*) and a continuance of the inner and outer layers in their separate sheaths to form the regenerated fascia lata. Soon the one layer (Fig. 3*C*) stops, but the other layer, the superficial one in this instance, continues onward, tapering more as it goes. This thinning out of the regenerated fascia allowed the bulging of the muscles of the thigh in this defect.

CASE 4.—Mr. A., aged 43 years, was operated upon Feb. 25, 1942, for a cure of a bilateral inguinal hernia, direct and indirect, combined. The ordinary Bassini technique was used without the use of fascia lata sutures. On Aug. 2, 1942, he was reoperated upon for a recurrence on the left side, and two pieces of fascia lata were used, each one-half inch wide

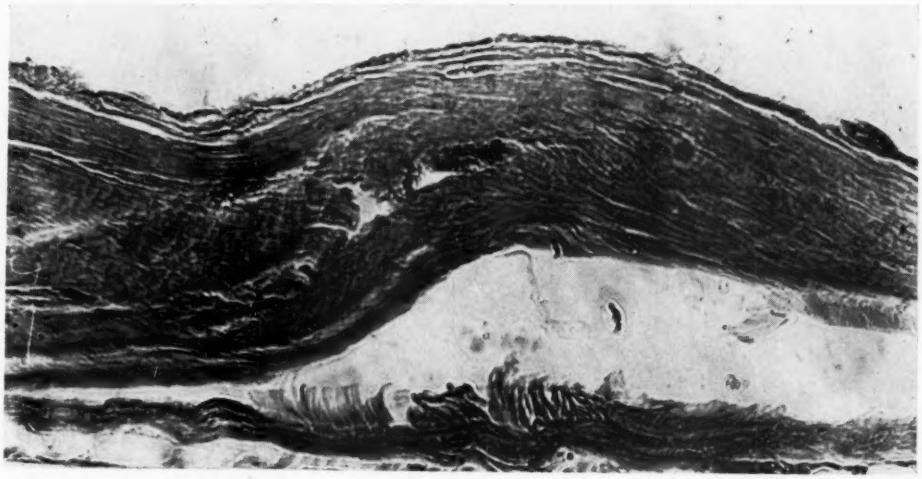

Fig. 4*A*.—Left half is the normal fascia lata, three layers; the right half is regenerated fascia lata, two layers.

and six inches long. They were removed from the left thigh. A cure resulted. Eight months later the patient permitted reopening of the thigh to obtain regenerated fascia for study. The old fascia margins had spread apart in the middle for a distance of two inches. The defect was filled in with a good, thick, shiny layer of fascia. The inner and outer layers appeared to be in continuity with the inner and outer layers of the normal fascia lata. A section three inches wide was taken transversely through the center of the regenerated area and it included 1 cm. of the margins of the normal fascia lata on its medial and lateral edges. In Fig. 4*A* are shown, in the left one-third, all three layers of the normal fascia lata margins well developed, with a part of the inner layer torn off as it was cut and mounted or otherwise, but it runs parallel to the main body of the inner fibers, and the middle layer terminates in the center of the specimen of the field. The inner and outer layers, which constitute the regenerated fascia, continued on for two inches or more across the defect (Fig. 4*B*) until they came to the fascia lata margin of the opposite side where the inner and outer layers continued on in continuity with the inner and outer layers of the normal fascia lata margin and the strong middle longitudinal bundles appeared again (Fig. 4*C*).

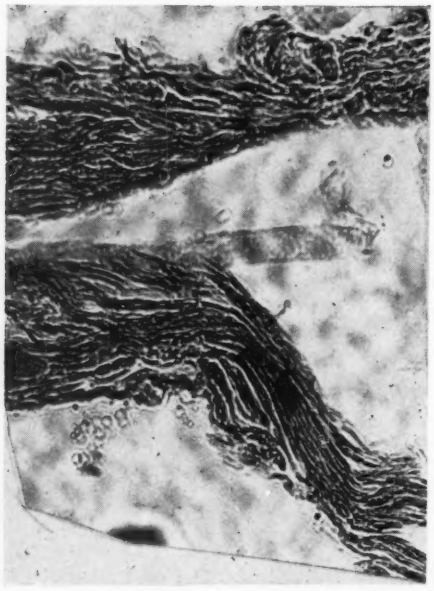

Fig. 4*B*.—Two layers of regenerated fascia lata.

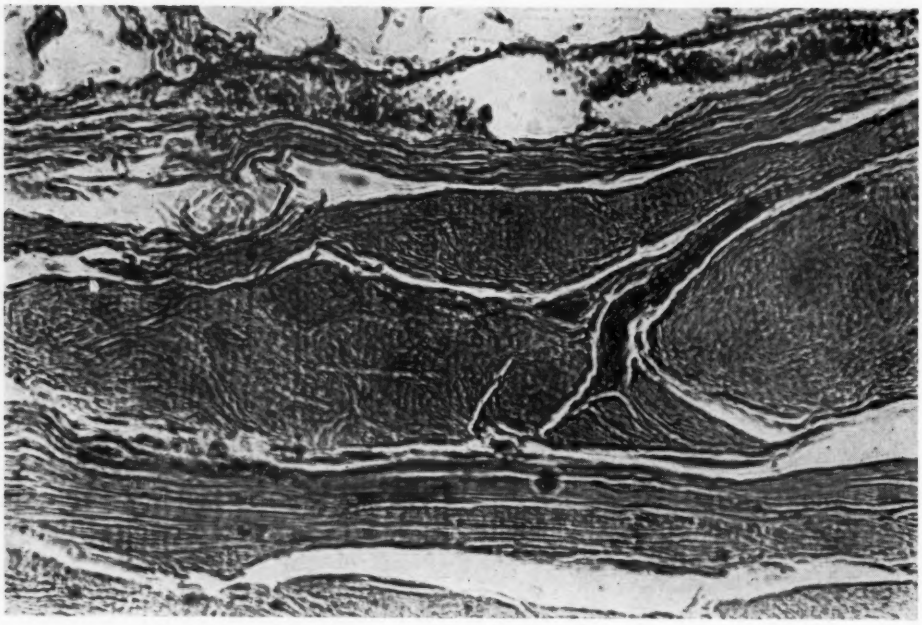

Fig. 4*C*.—Three layers of fascia lata margin.

CASE 5.—Mr. H., aged 62 years, had the most prominent role in all of the studies of the subject. In August, 1941, he submitted to operation for a cure of a right indirect inguinal hernia. Two wide, long pieces of fascia lata were removed from the right thigh for the repair. A third piece of normal fascia lata was removed for histologic study (which was described in Fig. 1 in the preliminary report[1] on this subject). On Dec. 5, 1943, this patient returned with a large indirect inguinal hernia on the opposite side. Operation for its cure was performed two days later, and again living fascia lata sutures were removed from the right thigh. The old skin scar was excised and the flap of skin, fat, and superficial fascia was carefully dissected back in one layer to expose below all the defect and regenerated fascia lata which had resulted following the previous operation of two years before. The following description was taken from the operative notes:

Remembering that this patient had rather thin normal fascia lata originally, it was thought that the regenerated fascia lata appeared nearly as thick as did the former normal fascia lata. The whole elliptical area was filled in with a layer of regenerated fascia at least three-fourths as thick as normal fascia lata and not quite as white. Grossly it did not contain visible longitudinal fibers, whereas they were plainly visible in the margins of the normal fascia lata.

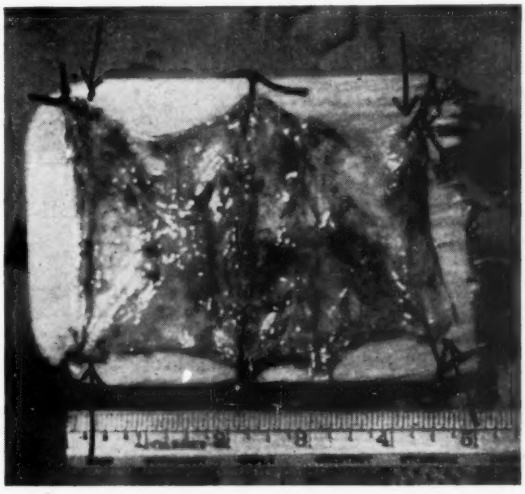

Fig. 5*A*.—Arrows point to narrow normal fascia lata margins; the wide intervening material is regenerated fascia lata.

An incision was made longitudinally parallel with the long axis of the defect along the mesial edge of the normal fascia lata, taking 1 cm. of that edge for a distance of three and one-half inches. A similar incision was made in the external shelf. A transverse incision was made at the ends of these two parallel incisions connecting them and thus freeing a block of regenerated fascia with 1 cm. of normal fascia lata attached to either side, the whole of which was three and one-half inches long and four inches wide. This regenerated fascia stripped off the muscle with the same ease as did the normal fascia lata. Grossly it had a visible capsule or sheath on its internal and external surfaces, of a glistening, grayish white color, which was in direct continuity with that of the normal fascia lata on both surfaces. The external surface contained a few tags of fat as did the normal fascia lata. The inner surface had a few fine trabeculae and small blood vessels extending to the muscles as did the normal fascia lata. Two long fascia strips three-eighths inch wide were taken from the remaining part of the lateral shelf of normal fascia lata to repair the hernia. (One of my colleagues, a former naval medical officer in World War I, who is marine minded, saw this specimen and remarked, "Now you have a specimen from shore to shore.")

In Fig. 5*A* is shown the gross specimen of regenerated fascia lata with a narrow rim of normal fascia lata on each side. The cutting of this specimen was ingenious and it was

Fig. 5*B*.—Left three-fourths is normal fascia lata margin with its three layers. The right one-fourth is the beginning of regenerated fascia lata, two layers.

Fig. 5*C*.—The two layers, inner and outer transverse, of the regenerated fascia lata.

cleverly mounted so that the full width of the specimen cut transversely was mounted in continuity on one large piece of glass, thus allowing microscopic study of the specimen from one end to the other. In Fig. 5*B* are shown the normal fascia lata margin of one side of this huge specimen with its three layers of fibers and the beginning of the regenerated fascia on the right comprised of its two usual layers, namely the inner and outer. In Fig. 5*C* is shown the continuation of these two layers for three and one-half inches until the other margin of normal fascia lata is reached with its three layers on the right (Fig. 5*D*).

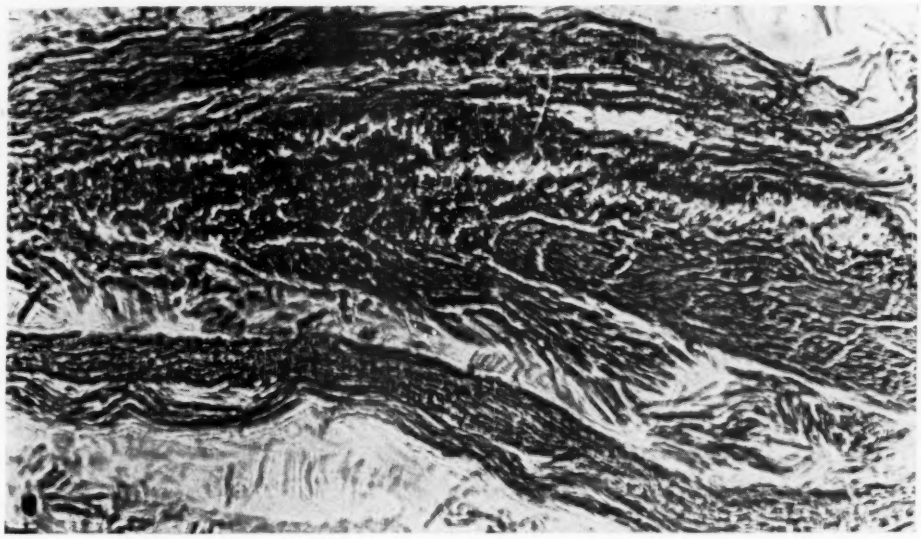

Fig. 5*D*.—The three layers of normal fascia lata margin in right half.

CONCLUSIONS

1. Regenerated fascia lata contains two layers, an inner transverse and an outer transverse layer. These two layers are in continuity with, and are direct extensions of, their corresponding layers of normal fascia lata which extend across the defect regardless of its size. Occasionally the transverse fibers do not run exactly at right angles to the longitudinal fibers. During an operative procedure when the fascia lata is dissected out, if one will observe carefully, the transverse layers will sometimes be seen to run somewhat obliquely to the long axis of the thigh. But the direction of the longitudinal fibers is constant.

2. It is never necessary to suture layers of fascia lata across the defect from which a transplant has been taken, or to make any effort to repair by one way or another the defect to prevent herniation. Herniation will be prevented by the newly formed regenerated fascia.

3. The more active is an individual, the more dense and better developed will be the regenerated fascia lata.

4. Regenerated fascia lata of six months to one year of age will be of sufficient density and tensile strength to be used successfully in certain surgical procedures in which, ordinarily, normal fascia lata is desired but lacking.

5. At first thought this work might appear to substantiate the work of Gratz[6] that fascia will develop anywhere in the body from muscle where fascia

is needed. In every instance of this work it is shown that the regenerated fascia layers are direct extensions across the defect of those corresponding layers of adjacent normal fascia lata. But the noticeable prominence of the thickness and density of the inner layer over that of the outer layer strongly suggests the importance of the proximity of muscle to the success of the fascia regeneration.

The author is grateful to Dr. Carl V. Weller, Chairman of the Department of Pathology of the University of Michigan for his personal attention to the cutting of the blocks of these specimens, and to Miss Evelyn Devine of his Department for the mounting and final preparation of the slides.

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ACUTE SUPPURATIVE PHLEBITIS COMPLICATED BY SEPTICEMIA

HAROLD NEUHOF, M.D., AND GABRIEL P. SELEY, M.D., NEW YORK, N. Y.
(From the Surgical Service and the Department of Laboratories, the Mount Sinai Hospital)

AS A CONSEQUENCE of the extraordinary results which are so often obtainable in the treatment of septicemia by the use of penicillin and of the sulfonamide drugs at this time there is an inevitable tendency to pay little or belated attention to lesions amenable to surgical relief. Among the latter is suppurative phlebitis of venous trunks. It may, therefore, be timely to present a study of this lesion based on ninety-three cases, the preponderance of which are certified instances. The importance of suppurative phlebitis as the feeding focus for septicemia was shown in its occurrence in one-fifth of 400 unselected cases of pyogenic sepsis.[1, 2] The extremely high mortality of unrecognized or untreated suppurative phlebitis which existed under such circumstances was an obvious challenge to diagnosis and therapy. Some influence on the mortality rate by operative treatment of suppurative phlebitis was demonstrable[2] in the period before, as well as in the earlier phases of specific chemotherapy. The question remains as to the role of surgery in the present phase of therapy by sulfonamide drugs and more particularly by penicillin. For its evaluation, more difficult than before, a full knowledge is required of the pathology, bacteriology, and clinical manifestations of suppurative phlebitis when complicated by septicemia.

It should be stated at once that the pathology of acute phlebitis uncomplicated by sepsis may be identical with that found in phlebitis from which septicemia is derived. Cases lacking all or many of the features of septicemia are not under consideration in this instance. There is also omitted an unusual but important group of cases of bland thrombosis characterized by chills and fever amenable to cure by venous ligation with or without thrombus extraction (to be reported elsewhere). The ninety-three cases will be analyzed according to etiology and pathogenesis, clinical pathology, bacteriology, topography, diagnosis, operative indications, and treatment.

ETIOLOGY

In the great majority of cases there was demonstrable a suppurative or acute inflammatory (often phlegmonous) focus in the immediate region of the large venous trunk which was the seat of phlebitis. It was a reasonable assumption that such foci (frequently suppurative lymphadenitis) were the sites from which the phlebitis was derived. These foci of infection were in turn derived from some more removed source of entry of infection into the body. Thus, a typical sequence of events was infection of a finger, lymphangitis of the arm, subpectoral suppurative lymphadenitis, suppurative thrombosis of the axillary vein, and septicemia. There are, of course, many instances in which such a clean-cut sequence of events is not apparent but some evidence of the etiologic relationship was to be found in almost all the cases in our series. It may be

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well to restate that we are concerned solely with phlebitis of substantial venous trunks. Phlebitis of venous radicles and often of small veins can be regarded as a part of the picture of any suppurative or phlegmonous lesion virtually anywhere in the body, is not recognizable as such clinically, and is not here under consideration.

The cases in our series are unselected and are listed as they occurred in a general hospital. As a result there is a considerable variety of venous trunks which are involved. The sites of suppurative foci from which main trunk phlebitis was derived also varied but can be placed in four groups (Table I).

Special attention should be called to a group of six cases in which suppurative phlebitis and sepsis followed either a cut-down intravenous infusion or repeated or prolonged intravenous infusion at a single site. It may be agreed that most of these patients were seriously ill and presumably prone to develop infection from an ordinarily trivial source. However, the infection is preventable by avoiding prolonged intravenous therapy at any one site. If the latter is unavoidable, the prophylactic administration of sulfonamide drugs or penicillin is warranted. In any event, the danger of septicemia from prolonged intravenous therapy at a single site should be acknowledged and combated.

TABLE I. SITES OF SUPPURATIVE FOCI FROM WHICH MAIN TRUNK PHLEBITIS WAS DERIVED

SITE	NUMBER OF CASES
In soft parts chiefly of extremities and neck	43
In region drained by the portal system	20
Otitic	20
Miscellaneous	10
Total	93

Another small but important group of cases, three in number, were those of phlebitis related to infections of long bones. Drainage of the abscess of the soft parts and of the bone in these cases did not influence the unfavorable clinical course inasmuch as suppurative phlebitis of substantial venous trunks was present in these cases. They are noted here because of the etiology and pathogenesis of the phlebitis.

In our series the etiology and pathogenesis was well illustrated by the appendical cases, six in number. In sequence to acute appendicitis there was a mesenteriolar abscess and phlebitis of the appendical veins which extended into the terminal branches of the ileocolic vein. From this area could be traced phlebitis of the superior mesenteric veins extending into the portal. The further sequence was liver abscesses, occasional phlebitis of the hepatic vein, and in some of the cases phlebitis of the inferior vena cava, abscesses of the lung, and pulmonary vein phlebitis with metastatic abscesses in the distribution of the systemic circulation.

Thus, the etiology of septicemia in all the cases of phlebitis of main venous trunks, ninety-three in number, was the phlebitis. The corollary was that cure could not be achieved unless the infected area of the vein was eliminated.

There was no demonstrable etiology for the suppurative phlebitis, such as an abscess in the soft parts, in only two of our cases. In both of these the femoral

and iliac veins were involved. Since all the other cases presented a more or less obvious etiology either during life or at autopsy, these two exceptions are worthy of some discussion. It would lead too far afield to discuss the subject of bland venous thrombosis (phlebothrombosis) in the lower extremities but we may state here that occasional cases presumed to be in this category proved to be cases of septic phlebitis. We shall report elsewhere that cultures of thrombi proved to be positive for pathogenic organisms in some of the cases of apparently bland thrombophlebitis. Finally, we have had the opportunity to follow the course in one case from bland thrombosis into extensive suppurative phlebitis of the popliteal and femoral vein. It will be noted that our only two cases of unknown etiology were femoral vein suppurative thrombosis. In the absence of other evidence we assumed that they represented the conversion from bland thrombosis of the lower extremities with that obscure etiology which characterizes other cases of venous thrombosis of the lower extremities.

CLINICAL PATHOLOGY OF SUPPURATIVE PHLEBITIS

An analysis was made of the reports on the infected veins filed in the Department of Laboratories with special reference to surgical implications. The specimens were obtained at operation or at autopsy. Obviously in the case of the former only limited study was possible. In the series of ninety-three cases only three without specimens were included. They were clearly cases of suppurative phlebitis, clinically and at operation.

It can be assumed that phlebitis of substantial venous trunks is derived from extension from smaller branches or from immediately adjacent suppuration. However, the pathway of the extension can be demonstrated only rarely. The gross pathology of acute infections of venous trunks is varied. We believe the lesions can be grouped into four characteristic macroscopic forms as follows:

1. The thrombophlebitic. A lustreless more or less thick-walled vein is expanded about its contained, often palpable, thrombus. The lesion usually is well circumscribed with a visible demarcation from adjacent normal vein. The length of the area of suppurative thrombophlebitis ranges from one-half inch to several inches or more. In the case of portal vein phlebitis the contents may be gangrenous and foul-smelling debris. However, the appearance in any case may be altered as the result of chemotherapy or penicillin. Thus, in a recent case of suppurative thrombophlebitis of the portal vein, the wall of the vein was considerably thickened and the contents were some fluid pus and firm, fleshy, thrombotic material.

2. The phlegmonous. The wall of the vein is grayish, hemorrhagic or necrotic, and is infiltrated. A visible thrombus may not be present. The lesion usually has an ill-defined limit.

3. The pyophlebitic. The wall of the vein usually shows only slight evidence of inflammation and at times so little that the discovery of pus within it is unexpected. The limits are ill-defined. In addition to fluid pus, small bits of thrombotic material may be found within the lumen.

4. The periphlebitic. The venous trunk is more or less embedded in inflammatory tissue. The wall of the vein is thickened, for the most part lustreless,

and may or may not contain a palpable thrombus. Usually it is difficult to determine if the change in the vein represents the alteration in the surface of any structure in contact with an inflammatory process or a phlebitis with or without thrombus involving all the coats of the vein.

The microscopic examination does not match the foregoing gross features. Although there are many variations in the picture, two main varieties can be described into which the cases can be grouped:

1. Acute suppurative phlebitis or suppurative thrombophlebitis; 84 per cent of the cases.

2. Acute phlebitis, endophlebitis, periphlebitis; 16 per cent of the cases.

With appropriate stains, bacteria can be discerned in varying numbers in the thrombi or in the walls of the infected veins. Indeed, the absence of bacteria should cast grave doubt in any given case as to septicemia having been derived from an infected venous trunk submitted to microscopic examination.

An analysis of our cases reveals extensive spread of suppurative phlebitis which usually takes place toward the later stages of the infection and as found at autopsy. In some of the patients operated upon relatively early in the stage of septicemia (or in a few instances in the preseptic stage) the suppurative phlebitis was sharply limited. Apparently the area of infection in the vein spreads rapidly in the middle and later stages of the disease. On the basis of a few observations it may be stated that in the case of portal vein phlebitis the lesion may be extensive even in the early stages of septicemia.

A study was made of the relationship, if any, between the types and extent of the pathology in the vein and clinical manifestations. In general no direct relationship could be discerned, although it can be said that the classical or typical picture of septicemia was most often seen in suppurative thrombophlebitis. Furthermore the blood culture features—positive or negative blood culture, number of microorganisms, variety of bacteria—bore no apparent relationship to the extent or severity of the phlebitic process.

Some aspects of the pathology are worthy of special mention because of their surgical implications. There were two cases in which the source of infection was adjacent to the axillary vein which, however, was by-passed or skipped, the subclavian vein being the seat of the phlebitic process. Perhaps the fulminating and rapidly fatal course in both cases was related to the unusual pathway of extension. In a case of suppurative pylephlebitis derived from an appendicitis, the superior mesenteric vein was by-passed. Thus, the possibility that phlebitis may skip a substantial or main venous trunk to be present at a more central and larger trunk must be borne in mind in order to avoid overlooking the lesion at an operation.

Phlebitis of a main venous trunk apparently derived from a crosscurrent infection may also occur. There was one striking instance in which the left renal vein was involved following a phlebitis of the right renal vein complicating a carbuncle of the kidney. This case also illustrated the fact already alluded to that severe phlebitis without thrombosis can occur and that the surface of the vein may not reveal a marked change in appearance.

When a branch close to a venous trunk is involved by phlebitis, extension to the parent vein can be regarded as virtually inevitable unless an operation is performed at an early stage of the infection and terminates the branch phlebitis. There was one case of branch vein suppurative thrombophlebitis in our series in which the inflammatory process seemed to terminate just short of the axillary vein. The gross appearance of the axillary vein was normal in this case. Since excision of the infected branch vein also resulted in cure and the vein at the site of section close to the axillary vein was normal, it is assumed that the phlebitis had not extended into the axillary vein.

BACTERIOLOGY IN RELATIONSHIP TO PROGNOSIS

The great preponderance of our cases antedates the period of chemotherapy and penicillin. The series should, therefore, be useful for comparative purposes. Blood cultures were taken in eighty-six of the ninety-three cases and were positive in fifty-four (Table II). The microorganisms found in the latter are grouped in Table III. The bacteria other than streptococci, and staphylococci included *Bacillus coli,* Friedländer's bacillus, *Streptococcus viridans* and enterococcus. Anaerobic bacteria were recovered in four instances and there were three cases in which two microorganisms were present in the blood stream.

TABLE II. ANALYSIS OF THE RESULTS OF BLOOD CULTURES IN 86 CASES; RELATIONSHIP TO MORTALITY

BLOOD CULTURES	NUMBER OF CASES	NUMBER OF DEATHS	MORTALITY PER CENT
Positive	54	37	68.5
Negative (portal vein phlebitis in 7 of these)	32	17	53

Evidence of septicemia at autopsy in all fatal cases of both groups.

TABLE III. MICROORGANISMS IN FIFTY-FOUR POSITIVE BLOOD CULTURE CASES

ORGANISM	NUMBER OF CASES	NUMBER OF DEATHS
Streptococcus hemolyticus (beta)	24	10
Staphylococcus aureus	13	12
Other microorganisms	17	15

The group of seventeen cases of portal vein phlebitis in which blood cultures were taken provides some special features. The blood culture was positive in ten of these cases. This high percentage is not in keeping with commonly held concepts which maintain that filterage by the liver commonly prevents general systemic invasion by the infecting organism. It is also maintained that a phlebitis of the hepatic vein should be postulated in cases of pylephlebitis in which the blood cultures are positive but hepatic vein phlebitis was not found at post-mortem examination in a number of our cases.

Negative blood cultures in pylephlebitis may be in the same class with negative blood cultures in suppurative phlebitis in systemic venous trunks. The latter, in the presence of evidence of septicemia (clinically or at autopsy), cannot be accounted for in an offhand manner. Indeed, there appears to be a school which believes and teaches that septicemia cannot be regarded to exist in

the absence of a positive blood culture. Thus, in the field of phlebitis of the lateral sinus there are those who believe that the diagnosis cannot be regarded as established or at any rate that surgical intervention is not indicated until a positive blood culture is obtained. It is, of course, fair to assume that if sufficient cultures are taken at frequent enough intervals microorganisms would be found in the blood stream in all cases. Table II is, therefore, of important clinical significance because it reveals the high proportion of negative blood cultures taken in the standard manner and with good technique in proved cases of phlebitis complicated by septicemia. It can be added that the mortality of this group would have been higher if some of the patients had not been cured by operation. If filtration by the liver does not explain negative blood cultures in suppurative pylephlebitis, what explanation can be offered for negative blood culture in suppurative phlebitis of systemic venous trunks? It appears to us to be logical to assume that the variety of phlebitis accounts for the presence or absence of bacteria in the blood. We believe that the type of phlebitis characterized by more or less obturating thrombosis or by "fleshy" and firmly adherent thrombi is the form or one of the forms in which blood cultures are likely to be sterile. It also appears reasonable to believe that blood cultures are more prone to be positive when the vein which is the seat of phlebitis is in a direct line with the flow of the blood stream rather than in an eddy or in a situation in which the venous pressure is high rather than low. In general, the nearer the heart the more definitive the suction action on the venous trunk, which is the seat of thrombosis, and the more one would anticipate a positive blood culture.

A study was made in order to learn if there were any correlation between the severity and extent of the phlebitis and the blood culture results. No correlation was found to exist. Thus, blood cultures were negative in not a few instances of the severest forms of suppurative thrombophlebitis. There was also no relationship between the number of colonies in cases of positive blood cultures and the extent of the lesion or the prognosis. As shown for septicemia in general,[1] there is to be noted in septicemia derived from suppurative phlebitis of venous trunks that fulminating cases may have few colonies and cases pursuing a relatively bland course may have many or even innumerable colonies.

TOPOGRAPHY

An analysis of the sites at which suppurative phlebitis was located in the ninety-three cases shows that a great many are readily accessible surgically

TABLE IV. ACCESSIBLE VENOUS TRUNKS INVOLVED BY SUPPURATIVE PHLEBITIS IN 43 CASES (OTITIC OMITTED)

Axillary vein	12
Other veins of upper extremity	7
Veins of lower extremity	8
Internal jugular vein	5
Other veins of neck	3
Facial vein	2
Iliac vein	2
Ovarian vein	2
Other veins	2

and that the continuity of none of the venous trunks (with the possible exception of the portal vein) was essential to life. Omitting the groups of lateral sinus and portal vein phlebitis, the readily accessible veins, situated chiefly on the surface of the body, are listed in Table IV. The large proportion of cases in which relatively simple surgical procedures can aid in the solution of the problem of septicemia thus becomes apparent.

DIAGNOSIS—OPERATIVE INDICATIONS

A diagnosis or presumptive diagnosis of suppurative phlebitis of a venous trunk as the cause of septicemia can be made in most instances, chiefly on indirect evidence. However, the diagnosis usually cannot be entertained in the absence of a determinable source of infection. It is, therefore, of interest to note that a definite source existed in eighty-three of the ninety-three cases (Table V). Usually the inflammatory mass or abscess was in the region of, or more often in juxtaposition to, the infected venous trunk (seven-eighths of the cases).

TABLE V. CLINICAL FEATURES POINTED TO AS THE SOURCE IN EIGHTY-THREE CASES

	NUMBER OF CASES
Abscess or area of suppuration	16
Inflammatory mass or cellulitis	16
Inflamed vein palpable as such	5
Mastoid or other osseous focus	32
Portal system: chiefly cholecystic or appendical foci	14
Subpectoral abscess or mass (special mention because of its importance and frequency)	9

The general clinical manifestations are those of septicemia and as such are not distinctive of phlebitis as the source. An analysis of the manifestations has already been made[1, 2] but was repeated for this series of cases. The classical febrile course was present in only one-half of the cases and chills occurred in only two-thirds of the cases. The blood culture was positive in five-eighths of the cases.

From the foregoing it appears that the diagnosis of suppurative phlebitis of a substantial venous trunk should be entertained in the presence of septicemia when a likely etiology exists and the inflammatory or suppurative focus is situated in the neighborhood of, or in immediate proximity to, such a venous trunk. We maintain that under certain circumstances to be set forth, surgical exposure for diagnosis and, in the presence of phlebitis, excision of the infected vein are warranted. In this connection the frequently made diagnosis of complicating bacterial endocarditis should be referred to since that lesion forbids surgical intervention because of its futility under such circumstances. We would emphasize the fact that the diagnosis cannot be made on the presence of heart murmurs and positive blood cultures, or even petechiae which may be of bacterial or nonbacterial origin. In any event the margin of error in the diagnosis of bacterial endocarditis is great and if an operation is indicated it should not be withheld unless the diagnosis of endocardial invasion is virtually certain.

INDICATIONS FOR OPERATION FOR SUPPURATIVE PHLEBITIS

In the period before sulfonamide and penicillin therapy the indications for operation were both precise and urgent in our opinion. The requirement was to eradicate if possible, and at the earliest moment, the area of the infected vein from which septicemia was derived. Indeed, the best results were obtained, as might have been anticipated, by operations performed in what may be called the preseptic phase or at any rate before sepsis was fully established. The indications now are profoundly influenced by sulfonamide and penicillin therapy since many cases will not require operation because cure is achieved by such therapy. Operation now is indicated only in those cases in which cure is not achieved. This does not refer to the drainage of an abscess or the eradication of a suppurative focus from which the phlebitis is derived because the indications for such drainage or surgical eradication remain unchanged. Concerning the phlebitis, however, the evidence is clear that healing will result so often that sulfonamide, and more particularly penicillin, treatment can be referred to as specific therapy in most cases. The important point today in the treatment of suppurative phlebitis which has produced septicemia is to identify in good time the patients who do not respond to that therapy and to operate on the vein under such circumstances. Much closer clinical observation is required in order to determine the progress of the case. Blood cultures may become negative during the spread of a suppurative phlebitis. Indeed, the evaluation of the clinical state during either penicillin or sulfonamide therapy requires an approach which comprises a considerable modification of previous thinking. A lack of appreciation of the extension of suppurative phlebitis may lead to the omission of, or too long-delayed, surgical intervention.

On the other hand, partial effects of sulfonamide and penicillin therapy warrant a more deliberate attitude toward surgical intervention than existed in the past. Thus, a delay in operation in a recent case, to which reference will be made, appeared to be justified. In another case operation was seriously entertained but further treatment with penicillin resulted in cure.

CONTRAINDICATIONS TO OPERATION

The question of general contraindication to operative treatment of suppurative phlebitis of large venous trunks warrants some discussion. The factor of bacterial endocarditis has been taken up. Otherwise the only general contraindication to be conceded is an evident hopelessness of a case because of its advanced stage. The argument that operation is not indicated unless the diagnosis of phlebitis is certain and not presumptive would result in the exclusion of most of the cases which might be amenable to surgical relief and the inclusion chiefly of cases too far advanced for surgical cure. There is the implication that a definitive operation for known phlebitis can be justified, but that an exploration of a venous trunk in the midst of an inflammatory area is meddlesome, may lead to untoward results, and is unwarranted. It appears to us that precise, nontraumatic surgical dissection will not open significant areas of infection and we have not noted ill effects in a number of instances of negative ex-

plorations for suspected phlebitis. In any event an appreciation of the little which might be lost compared with what might be gained in the treatment of an otherwise probably fatal condition should counterbalance that argument. A general contraindication to radical operation (excision) of the large venous trunks of the extremities rests on the assumption that considerable edema would follow. In the first place the primary assumption is false because edema is due to lymphatic blockage and not to the occlusion of a vein. Thus, many cases of ligation of the femoral vein for bland thrombosis in the lower extremities are not followed by edema. Second, excision of venus trunks may or may not be followed by edema, depending on the subsequent adequacy or inadequacy of lymphatic flow.[3(a)] One of us has reported[3(b)] a series of cases of excision of the axillary vein in radical operation for cancer of the breast in which edema of the arm did not result in the majority of instances. Third, the periphlebitis associated with most cases of suppurative phlebitis could undoubtedly be the cause of edema from lymphatic obstruction in not a few cases if recovery without operation should in fact occur.

Concerning surgical intervention on the portal vein it can be said that life is compatible with its occlusion unless closure is too abruptly induced in the normal vein because a collateral circulation can and does form rapidly.[4] Collateral circulation can be assumed to exist by the time operation is considered because the lesion of the portal vein usually is a more or less occluding thrombophlebitis, which has led to the opening of collateral hepatopetal vessels. Thus, ligation or drainage or a combination of both performed on the portal vein cannot be regarded as contraindicated in pylephlebitis on the basis of the danger of death resulting from the procedure.

OPERATIVE TREATMENT—EXCISION OF VENOUS TRUNK

It is impossible to ascertain if there is an accepted method of surgical treatment of suppurative phlebitis because of the virtual absence of any literature on the subject. Indeed, excluding operations on the lateral sinus and the ovarian vein it is only from personal communications that one can learn that any form of surgery for suppurative phlebitis has been attempted in the presence of septicemia. One of us has advocated[5, 6] the principle of excision of the infected vein as the logical method of treatment but is unaware of the acceptance of that method. Ligation of the vein proximal to the site of phlebitis has been recommended but we believe this to be inadequate because the infection (and suppurative phlebitis) is not prevented from extending through collateral branches, and the suppurative focus is permitted to remain in place to spread locally at will. In the otologic field, where excision is not feasible, a compromise procedure consisting of unroofing the infected lateral sinus (with or without ligation of the jugular) often has yielded satisfactory results. Simple proximal ligation may produce results which were unobtainable before because of sulfonamide or penicillin therapy. This does not seem likely to us, however, as operation will probably be indicated because (1) the suppurative phlebitis does not respond to that treatment at which time excision, whenever feasible, is indicated or (2) the septicemia is controlled but the phlebitic area is converted into a

collection of pus and exudate from which infection continues and for which ligation would be ineffective. Under these circumstances drainage may be indicated rather than excision, particularly when excision is a formidable procedure. Only drainage could, of course, be considered when excision is not possible as in the case of pylephlebitis.

Some principles for excision of infected venous trunks appear worthy of note even though the procedure is indicated less frequently than heretofore. Adherence to them has yielded a measure of good results in the past and they are equally applicable today, in our opinion. Perhaps the most important principle is not to be satisfied with the drainage of a collection of pus in the neighborhood of an accessible venous trunk when the clinical picture points strongly to septicemia. The first principle then is the exposure of the vein in question by precise surgical dissection at or in the area of infection. The exposure should be liberal but should extend through normal planes only enough to reveal a normal portion of the suspected vein. The dissection of the vein is then continued through the area of infection, the vein often being embedded in inflammatory tissue or exudate. The next principle is perseverance in the dissection of the vein throughout most or all of the area in which it is embedded with severance of intervening structures (muscles, etc.) if necessary. Only by means of such a dissection will limited thrombophlebitis or phlebitis with relatively insignificant external alteration be discerned. Complete dissection of the vein into normal areas at both ends and complete excision whenever possible comprises the third principle. Only by complete exposure can the limits of phlebitis be identified and thrombosis involving branches of the parent trunk cared for. Complete excision should be carried out whenever feasible regardless of the size or importance of the venous trunk—for example, excision of the subclavian into the innominate vein—because timely eradication of the lesion will cure the septic state.

RESULTS OF OPERATIVE TREATMENT

Operative treatment of some sort was employed in forty-three cases (lateral sinus cases are omitted) in which suppurative phlebitis of accessible veins existed. All cases are included whether or not operation was performed on the infected vein. In Table VI is revealed the significant fact that operations limited to drainage of the suppurative focus from which the phlebitis was derived were never followed by recovery. The contrast between the futility of drainage without surgical treatment directed toward elimination of the phlebitic focus and the results of combining both, particularly when adequate excision of the vein was

TABLE VI

	CASES	RECOVERED	DIED
I. Excision of veins in addition to drainage of causative abscess			
A. Adequate excision in accordance with described technique	16	14*	2
B. Inadequate excision or excision late in the disease	15	8	7
II. Operative procedures on the suppurative foci but not on the involved veins	12	0	12

*One patient died subsequently of an unrelated disease.

performed, also is apparent in the table. This conclusion today would probably hold only for cases in which the infection in the vein was not amenable to drug therapy. The twenty cases of phlebitis of the sigmoid sinus are omitted because their analysis requires considerations related only to the otologic field. It is interesting to note, however, that good results were obtained in this field in which the management of the problem of phlebitis is much more difficult than in general surgical fields and that radical excision which at least at times can be carried out elsewhere cannot be performed safely on the lateral sinus.

With emphasis on the fact that this study is based solely on phlebitis of major venous trunks we report the results of therapy by sulfonamides in our series of cases despite surprisingly poor results (Table VII). The number of cases is not large and better results might be anticipated in a larger or perhaps more representative series. All cases in which sulfonamides were not administered in adequate dosage are excluded. The apparent lack of any significant relationship between the blood culture findings and the results will be noted.

TABLE VII. THE INFLUENCE OF SULFONAMIDE THERAPY IN FOURTEEN CASES OF PHLEBITIS OF MAIN VENOUS TRUNKS COMPLICATED BY SEPTICEMIA

BLOOD CULTURE	NUMBER OF CASES
Positive	8
Ineffectual in all	
Negative	6
Ineffectual in 4	
Questionable efficacy in 2	

The results of excision in relationship to the blood culture and pathology of the infected vein can now be tabulated (Table VIII). Here again the series is not large and different results might be obtainable in a larger and more representative series or one in which excision had been carried out more promptly than was possible or deemed advisable in this series. The table also shows that there is slight relationship of the pathology or the findings on blood culture to the results which were achieved. The prognosis of suppurative phlebitis of main venous trunks complicated by septicemia appears to be related largely if not solely to the duration of clinical manifestations at the time of operation and to the accessibility of the infected vein and feasibility of adequate surgical treatment.

Reference has been made to the profound influence penicillin has had on the problem of sepsis-producing phlebitis. Up to the present time we have seen

TABLE VIII. PATHOLOGY AND BLOOD CULTURE IN RELATIONSHIP TO THE RESULT

	CASES	RECOVERIES	DEATHS
Positive blood culture			
Suppurative phlebitis	4	2	2
Negative blood cultures			
Periphlebitis	3	3	
Suppurative phlebitis	6	6	
No specimen	1	1	
Blood culture not awaited before operation			
Postoperative culture negative			
Suppurative phlebitis	2	2	

no instances in which cure has not been achieved when the infection is amenable to penicillin therapy. Penicillin has proved to be far more effective than the sulfonamides and the foregoing statistics (Table VII) would almost certainly have been far better had the patients been treated with penicillin. It is, however, apparent that, as in the case of the sulfonamides, there will be cases of failure or partial results by penicillin therapy, in which operation on the vein will be indicated. In a recent case of pylephlebitis (not in this series) sulfonamide therapy was employed over a long period of time. There was improvement in the clinical course (and negative blood culture) despite the known presence of suppurative hepatic foci. Finally, operation was performed on the portal vein consisting of drainage of pus from the lumen. Parallel experiences with parallel operative indications and procedures in the case of penicillin can be anticipated.

SUMMARY AND CONCLUSIONS

1. In the prepenicillin period, suppurative phlebitis was a common cause of fatal septicemia; in the present period it is often in an abortive form because of penicillin therapy. Suppurative phlebitis remains the common cause of septicemia.

2. The diagnosis of suppurative phlebitis producing septicemia often must be made on indirect evidence: an inflammatory focus (present in seven-eighths of the cases), chills (in two-thirds of the cases), and positive blood culture (in five-eighths of the cases).

3. Drainage of the suppurative focus will not suffice unless there is added thereto adequate excision of the main involved venous trunk. The combination of these procedures resulted in cure in 87.5 per cent of cases.

4. In the penicillin (and sulfonamide) era, fewer cases will be encountered in which surgical considerations will arise. In penicillin-resistant cases or in cases of partial results, the same principles of surgical treatment which have been laid down should be applied.

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THE AMBULATORY TREATMENT OF PHLEBITIS, THROMBOPHLEBITIS, AND THROMBOSIS WITH COMPRESSION BANDAGES

OTTO MEYER, M.D., NEW YORK, N. Y.

TREATMENT of acute and chronic phlebitis with pressure bandages has been very successful and has been in use in nearly all European countries for two decades.

Compression bandages have been recommended by many authors for the treatment of thrombosis and the prevention of pulmonary embolism. Castleman, from autopsy studies, has found the source of pulmonary embolism to be in the deep veins of the legs in approximately 95 per cent of the cases.

Lately compression bandages have been used in this country prophylactically. Ochsner stated, "There is only one treatment for pulmonary embolism and it is prophylaxis. A great deal can be accomplished by preventing the clot originally, as the authors have emphasized. It is my belief that every patient past 45 years of age who has to be operated on should have his extremities wrapped from his toes to his groin before he goes to the operating room. This wrapping is maintained during his postoperative period until he is able to move his extremities actively. Early ambulation has undoubtedly done a great deal to cut down the incidence of postoperative thrombosis."

Peripheral phlebitis is located chiefly in the legs, because the mechanism of the venous circulation favors infection of the veins of the legs. To meet the problems involved in the treatment of peripheral phlebitis we must have a clear conception of the factors which force the venous blood to flow back to the heart.

Besides the contraction of the left ventricle, the vis a tergo, and the negative pressure within the chest which sucks the venous blood into the thorax, the massaging effect of the skeletal muscles is of utmost importance. The pressure of the contracting muscles on the veins pushes the blood to the heart, because the valves of the veins permit movement of the blood only in this direction and prevent its backflow to the tissues. The muscles, therefore, act as subsidiary pumps which aid materially the flow of the venous blood, especially during muscular exercise.

The effect of muscular exercise on the venous flow can be demonstrated easily in bloodletting from the vein in the elbow. The blood flows more freely when the patient opens and closes his fist, thus exercising the muscles of the forearm. Each contraction of these muscles exerts a pressure on the underlying veins and increases the flow of venous blood to the opening of the needle.

But in spite of increased muscular contraction of the forearm muscles, much pressure energy is lost into the empty space. I was able to demonstrate how a materially increased venous flow can be achieved by application of elastic

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bandages around the forearm. After the bandages are firmly (naturally centripetally) applied, all the pressure energy can be concentrated on the deep veins.

If there is insufficient activity of the skeletal muscles of the legs, as in persons who stand much during their working hours, or who do little walking, a venous congestion develops in the legs and creates a *locus minoris resistentiae* to infection.

It is well to note that Krogh has pointed out that a relatively small elevation of venous pressure must cause fluid to accumulate in the tissue spaces. An example of this is that the erect human being is constantly near to edema.

Then, when the veins have become infected, the venous congestion becomes permanent and more pronounced. The inflammatory swelling of the inner coat of the veins and the formation of blood clots decrease the diameter of the veins. A permanent phlebostenosis develops which decreases the capacity of the veins to carry a normal volume of blood from the tissues to the heart, thus producing a permanent venous congestion in the affected area which weakens the tissues to such an extent that they cannot overcome the infection.

The tissue in an area of venous congestion is affected by retardation of the circulation which results in accumulation of carbon dioxide, accumulation of metabolites, and stagnant anoxia.

When the capillary walls are exposed to oxygen lack, in the frog even for as short a time as three minutes, they are damaged and become permeable to protein.

Impairment of venous drainage increases venous pressure which results in increased transudation into the tissue spaces. Increased pressure in tissue spaces creates pain by compressing nerve tissue.

The local effect of stagnant anoxia is often responsible for necrosis and ulcer formation in a congested area.

Allergic reactions, according to Knepper, are especially severe in a congested area with retarded circulation. The interaction between antigen and antibody is dependent on the time factor. In a congested tissue, therefore, we find allergic reactions of the skin in the form of congestive dermatitis and congestive eczema.

As the venous congestion is the principal factor which prevents the elimination of the infection from the veins, the customary method of treating phlebitis is useless, because it does not attack the venous congestion. Removal of the venous congestion is the "*conditio sine qua non*" for a cure of peripheral phlebitis. In the customary treatment of phlebitis the patient is confined to bed for a long period of time with the leg fixed in an elevated position. All that can be accomplished by the rest cure is a temporary improvement, but never a cure. Unless the venous congestion in the legs is removed, a cure is impossible.

For this reason the anticoagulant therapy, with heparin and dicumarol, and the ligation therapy have not been very successful in the treatment of thromboses and in the prevention of embolism.

In treating phlebitis of the legs two purposes must be achieved at the same time. One is to cure the phlebitis by removing the venous congestion. The other is to prevent the detachment of a blood clot. Both purposes are achieved by the use of pressure bandages.

It was the merit of H. Fischer to have originated the ambulatory pressure treatment of phlebitis. Fischer observed that in the treatment of leg ulcers inflamed superficial veins healed remarkably fast under compression bandages. This observation encouraged him to treat also the inflammation of deep veins with compression bandages.

Fischer's method was devised with the aim of eliminating embolism and progressing thrombosis. By applying a strong and even pressure around the leg to a point above the inflamed vein, he succeeded in compressing the dilated veins, thereby restoring function of the valves and normal circulation. The pressure also promotes the absorption of existing thrombi and prevents their detachment from the walls of the veins. The restoration of the circulation prevents formation of new thrombi and removes the swelling. Fischer emphasized that the action of the pressure bandage is increased manifold by walking, because the contraction of the muscles empties the veins (that have been compressed sufficiently by the bandage to restore the function of the valves) in the direction of the heart, thereby promoting circulation.

A former pupil of Fischer, I developed in 1930 a modification and simplification of the original Fischer treatment. In the treatment of acute and chronic phlebitis of the legs I used successfully for fifteen years the elastic combination bandage. I saw not a single case of embolism in a very large number of phlebitis cases. The combination bandage consists of a 4-inch wide, moist, medicated, viscous, nonsetting, zinc-gelatine type bandage (Contura bandage) and a 3-inch wide, elastic, adhesive pressure bandage (Pressoplast bandage). The elastic adhesive bandage is used for compression and grip. It has a soft, nonfray edge.

For diagnosis and treatment the patient lies on a flat table.

The diagnosis of phlebitis and thrombophlebitis of the deep veins of the leg is made by deep palpation with relaxed muscles. Ochsner stated that the veins in thrombophlebitis and phlebothrombosis are tender and sensitive to pressure. Healthy normal veins (for example, dorsal hand veins) can stand much pressure without any pain. It is always necessary to examine both legs, as we deal in most cases with a horseshoe phlebitis. Phlebography is not without danger and not as accurate as the diagnosis by deep palpation.

The technique of the combination bandage is as follows: After protecting ankle and knee, the physician covers the leg loosely with a contura bandage. Then, over the contura bandage, he applies a three-inch wide pressoplast bandage with strong, but nonconstricting, pressure.

The combination of the medicated contura bandage and the elastic pressoplast bandage provides an elastic compression which is adaptable to the function of the muscles and joints. The moist, viscous, antiphlogistic contura bandage does not become stiff like Unna's paste bandage, and it moves freely with the muscles. The medication in the contura bandage prevents irritation

of the skin so often seen after the direct application of the elastic adhesive bandages, and it makes a comfortable treatment, even of long duration, possible. Also, the change of the bandage is easy, as the contura bandage does not stick to the hair of the leg. Therefore, shaving of the leg is not necessary.

The application of the combination bandage (contura plus pressoplast) incorporates all the advantages of Unna's paste bandage and the elastic adhesive bandage without their disadvantages. The contura bandage remains wet and pliable under the pressoplast bandage. The soothing antiphlogistic medication of the contura bandage protects the skin and facilitates the removal of the bandage.

In treating the legs below the knee, the bandage is started directly behind the toes and is wound up to the knee. The bandages are wrapped around the leg in the direction of the heart. They must cover the foot, heel, and calf. Only the toes remain free.

In treating the thigh, the bandage starts with strong pressure as high as possible near the Poupart's ligament and is wrapped around the thigh in the direction of the knee to a point directly above the knee. In order to prevent detachment and passage of a thrombus, it is necessary to apply several layers of pressoplast bandage with maximal pressure at the upper (proximal) end of the thigh.

The knee remains, as a rule, free. If it is necessary to bandage the knee, the technique is the same as previously described. After the popliteal space has been well padded with cotton, the contura bandage is applied loosely, and then the pressoplast bandage is applied under "optimal" pressure.

The pressure must be even and the tension of the bandage must be considerable. A loosely applied bandage fails to relieve symptoms. In the pressoplast bandage the combination of the particular adhesive spread with the remarkable stretch and regain properties of the cloth makes it possible to provide the exact degree of compression and grip.

If the correct pressure has been applied, the patient will feel a relief of pain immediately. If the pressure is too strong, the patient will complain about severe pain almost immediately after the bandage has been applied. He can bear excessive pressure for only a few minutes. If the bandage is too loose, the pain which the patient felt before application of the bandage will not stop. Then more pressure must be applied.

In almost all cases of phlebitis of the legs it is necessary to apply the bandage not only to the lower part of the leg, but also to the thigh, even if there are no apparent signs of phlebitis in the thigh. Careful examination by deep palpation at the middle of the thigh will disclose in almost all cases an inflammation of the deep femoral vein. It is obvious that the inflammatory swelling of the femoral endothelium interferes with the drainage of the venous blood and produces congestion in the lower leg.

It need hardly be mentioned that this method can be applied only in cases of phlebitis where the thrombosis does not involve the large vessels of the abdomen.

The Fischer treatment is contraindicated in the very rare cases of purulent thrombosis.

After application of the bandage the patient is told to walk as much as possible, at least three miles daily, and to avoid standing.

Muscular contractions during walking result in the effect of positive pressure. Muscular relaxation during walking produces negative pressure. The alternate contraction and relaxation of the muscles create a difference in pressure which is the deciding factor for the promotion and acceleration of circulation in all blood vessels.

The bandage is changed at first every third day, and later twice weekly. The swelling decreases rapidly under the bandage, especially the often enormous edema found in acute phlebitis. In these cases the bandage must be renewed as soon as it becomes loose, if necessary daily for the first days. It cannot be stressed enough that the bandages must always fit snugly and tightly. If this rule is not observed, detachment of a thrombus with subsequent pulmonary embolism may result.

Pain disappears as a rule immediately on application of the bandage, or at least decreases considerably. There is practically no danger of embolism if the bandage is applied with sufficient pressure and up to a point above the thrombus.

The modified Fischer treatment with the contura and pressoplast bandages is effective in acute, chronic, and latent phlebitis, and in their complications, namely, phlebitic ulcer and phlebitic eczema. It also is effective in most cases of varicose ulcer and varicose eczema, because varicosity is mostly complicated by a latent phlebitis in the deep veins, and the pressure bandage will remove the congestion in the legs.

In treating ulcers and eczemas of the leg with the modified Fischer treatment, the ulcer or eczema is covered first with a suitable ointment (cod-liver oil) and a piece of gauze. Then the contura and pressoplast bandages are applied as described previously.

The results with the ambulatory pressure treatment, based on Fischer's principles, have been confirmed by Wright and many other authors.

H. Fischer reported in 1924 that he had treated 2,400 patients with phlebitis without a single embolism.

E. Fischer, the son of the originator of the treatment, treated 2,000 patients with phlebitis and thrombophlebitis without a single case of embolism.

Eichenlaub reported in 1931 that he had treated several hundred patients with thrombophlebitis with the Fischer method without a single case of embolism.

Stotzer treated over 1,000 patients with phlebitis with compression bandages and did not have a single case of embolism.

Leun reported in 1941 that in the Gynecological and Obstetrical Clinic of the University of Giessen after the systematic prophylactic application of pressure bandages (in 1933), 6,033 maternity patients were delivered without a single fatal case of embolism, and that 7,034 gynecologic patients were operated

upon with only twenty-two (3.1 per thousand) deaths from embolism, representing a decrease of over 50 per cent of the mortality rate from embolism as compared with the period before the prophylactic treatment with pressure bandages was introduced.

Kretzschmar reported in a lecture on phlebitis at a meeting of the Hollywood Academy of Medicine in 1930 that during the past nineteen years he treated a large number of phlebitis patients in accordance with Fischer's directions without one fatal issue and without one case of embolic pneumonia.

Eichenlaub stressed the following advantages of the Fischer treatment: shorter hospitalization, no necessity of rest in bed, prompt relief of pain, shorter duration of disability, avoidance of the complications seen in cases of thrombosis which have been healed by rest in bed, such as blood and lymph congestion, ulcerated legs, inflammatory changes of the joints, flabbiness of all the muscles and ligaments. He further mentioned it as useful in preventing thromboses if used before delivery and operations, or also directly afterward. He stated that the compression restores the function of the valves of the veins, increases the compression and suction effect of the contractions and relaxations of the muscles in motion, and induces and increases the circulation.

He stressed the necessity of early treatment in order to obtain good results. The advantages of this treatment are: the patient is completely cured (*restitutio ad integrum*), and he can immediately leave the bed and walk around. Slight increases in temperature due to the thrombosis are no contraindication. The compression must be firm enough, then the pain is immediately relieved. If there was fever at the start of the treatment it will soon disappear. If it is necessary for the patient to stay in bed because of another condition, active and passive leg exercises are necessary several times daily, in order to prevent spreading of the thrombosis and also to effect a cure which, however, will take more time to effect than if the treatment is ambulatory. If the thrombosis has already spread into the abdominal cavity, the patient must at first stay strictly in bed with the legs elevated. After a period of time which varies individually in every case, a compression bandage can be applied to the abdomen in order to shorten the duration of the rest in bed. The ideal of all therapy, *cito, toto, jucunde*, is also, and especially so, the ideal of pressure therapy.

Hohmann recommended the pressure bandage treatment of thrombophlebitis very highly and believed in time every physician will use it.

The fact that the venous congestion creates a *locus minoris resistentiae* to infection in the veins of the legs makes it imperative to prevent reinfection from sources of infection elsewhere in the body while treating the peripheral phlebitis locally with pressure bandages.

In my paper on "Latent Phlebitis as a Cause of Rheumatism" I stressed the importance of oral infections as a cause of jugular phlebitis and peripheral phlebitis.

It has been proved pathologically by Dietrich, Siegmund, and Hall that acute infections spread from tonsils, teeth, and the pharynx to the jugular veins by way of the small connecting veins, establishing a secondary focus in the jugular veins.

To cure phlebitis in the legs the physician must eliminate infectious foci in the mouth cavity, as infected (especially pulpless) teeth and infected tonsils. I pay special attention to infected tonsil stumps. Since a great number of tonsillectomies are done incompletely, the physician should always think of this possibility. I had infected tonsil stumps removed in over 500 phlebitis patients. This procedure shortened the treatment of phlebitis in each case considerably.

In a paper on the eliminating function of the tonsils for dental infections, I explained how removal of infected (especially pulpless) teeth may clear up a coexisting tonsillitis.

After removal of the primary oral foci the secondary focus in the jugular veins disappears sometimes immediately without further treatment. The diagnosis of jugular phlebitis is dependent on tenderness of the jugular veins. On deep palpation sometimes an induration is felt by the palpating finger. If the infection in the jugular veins persists, leech treatment has proved successful in removing the secondary focus. I have used this method nearly daily since 1937.

In numerous papers I have emphasized the importance of removing the primary oral foci of infection and the secondary focus in the jugular veins for the treatment of peripheral phlebitis.

Removal of the primary and secondary foci is also one of the surest measures to prevent peripheral phlebitis. Ochsner and DeBakey stated, "Infections are contributory in the production of distant thromboses, because of the changes in the blood constituents resulting from destruction of tissue. For this reason, it is prophylactically desirable to remove all foci of infection whenever possible."

I agree with Robinson, who stated, "Pulmonary embolism rarely occurs unless some sort of phlebitis, usually phlebothrombosis, exists. The real prevention of embolism therefore resolves itself into prevention of phlebitis."

SUMMARY

The successful treatment of peripheral phlebitis hinges on one factor mainly, the elimination of the venous congestion in the affected area.

The venous congestion of the leg is eliminated by the ambulatory treatment.

The ambulatory treatment consists of the application of pressure to the leg with the combination bandage (contura plus pressoplast), and regular daily walking exercises.

The treatment cures the phlebitis in the leg by eliminating the venous congestion, thereby removing the *locus minoris resistentiae* and making it possible for the affected tissues to overcome the infection.

The treatment practically prevents embolism.

The treatment must be supplemented by the removal of primary foci in the oral cavity and secondary foci in the jugular veins to prevent reinfection of the veins of the leg.

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MULTIPLE RETROGRADE SAPHENOUS VEIN LIGATION AND PHLEBECTOMY WITH AID OF MALLEABLE INTRALUMINAL GUIDE

ARKELL M. VAUGHN, M.D., CHICAGO, ILL.

(From the Department of Surgery, Loyola University School of Medicine and Mercy Hospital)

HIGH saphenous vein ligation combined with multiple retrograde ligations and excision of segments of the vein is superior, in my experience, to high ligation plus retrograde injection of a sclerosing solution.

In this procedure locating the saphenous vein above the knee is often difficult, especially in obese patients. To overcome this difficulty a malleable intraluminal guide, such as a flexible medium-sized uterine probe, is inserted into the lumen of the vein near the fossae ovalis area and passed downward. The vein is easily located over the probe above the knee and can be readily dissected out. This procedure can be repeated down the course of the vein above and below the knee. This maneuver has aided in vein operations and it is presented here to other surgeons for their evaluation.

For several years, high ligation was combined with retrograde injection of a sclerosing solution. It was observed that patients who received retrograde injections were, for the first few days, more uncomfortable and disabled than were those who had ligation only. This was due to a chemical phlebitis which in some instances was quite severe. It was observed further that many patients who consulted me two or more years after operation elsewhere with retrograde injection had large recurrent varicosities either above or below the knee or both. Many times re-operation revealed that recurrence was due to inadequate surgery at the first operation. Large incompetent external or internal femoral cutaneous veins arising near the fossae ovalis were found. These had not been ligated previously and subsequently dilated. In some instances the saphenous had been entirely overlooked, but a rather large external or internal femoral cutaneous ligated, in the belief that the saphenous vein was being ligated. The reason for recurrence in these cases was obvious.

Another group of patients observed were those who had been operated upon previously with meticulous care. All the branches entering the saphenous at the fossae ovalis had been ligated and four to six inches of the vein had been resected distally. Up to 10 c.c. of a sclerosing solution had been injected into the distal part of the vein. Many of these patients returned in two years or more with recurrences below the knee and occasionally both above and below the knee. The recurrence in these cases was not due to inadequate previous surgery but, in my opinion, to incompetent communicating veins, or recanalization of the thrombi following the retrograde injection, or possibly a combination of both.

Still another group of patients were those who presented themselves with recurrences, who had previous ligation and injection elsewhere by competent

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surgeons in recognized clinics and hospitals. Recently one of these patients who had been operated upon four years before, with recurrence, was re-operated upon. The fossae ovalis area was re-explored and nothing found except a fibrous cord which represented the previous ligated and injected saphenous vein. This fibrosed vein extended about six inches below the fossae ovalis and then began to dilate and presented a varicosed vein both above and below the knee. A cross section of the vein in the thigh (Fig. 1) above (Fig. 2) and below the knee (Fig. 3) revealed that in the thigh the vein was almost completely fibrosed, there being a very small lumen in its center (Fig. 1). Above the knee one side of the vein showed evidence of previous thrombosis which was organized, but was greatly dilated (Fig. 2). Below the knee the vein was greatly dilated with evidence of previous thrombosis (Fig. 3). The recurrence in these cases above or below the knee was not due to inadequate surgery, but in my opinion to a recanalization of the thrombus, possibly aided by incompetent communicating and perforating veins.

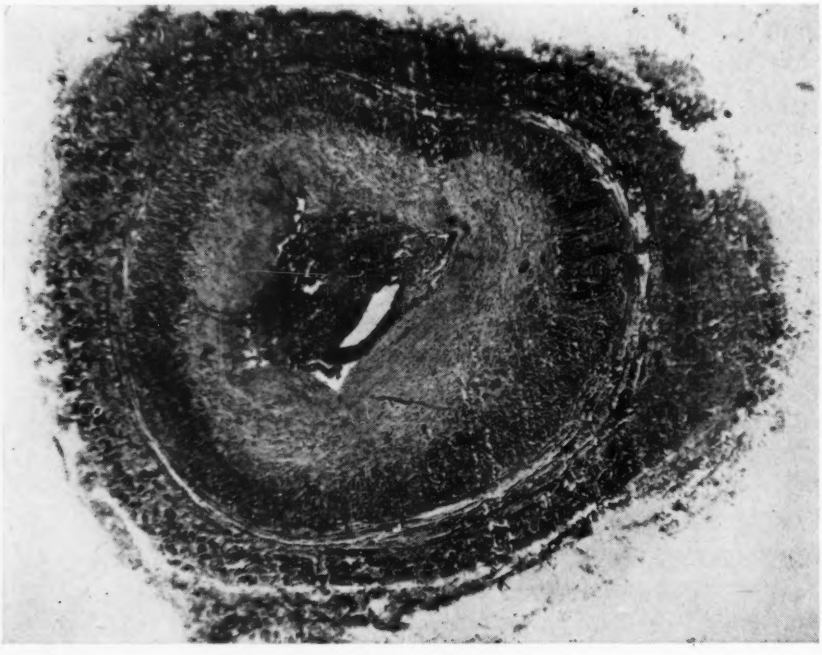

Fig. 1.—Cross section of saphenous vein in the upper thigh about four inches below fossae ovalis. A thorough ligation with retrograde injection was performed four years previously. Note the organization of old thrombus and canalization.

From these observations it was concluded that recurrences above and below the knee were not always due to inadequate surgery or collateral proliferation, but to a recanalization of the thrombosed vein which was possibly aided by an incompetent communicating or perforating vein down the course of the vein.

Consequently, it was decided to attempt retrograde ligation with excision of segments of the vein both above and below the knee along with high saphenous ligation rather than retrograde injection. This I have been doing for the past five years.

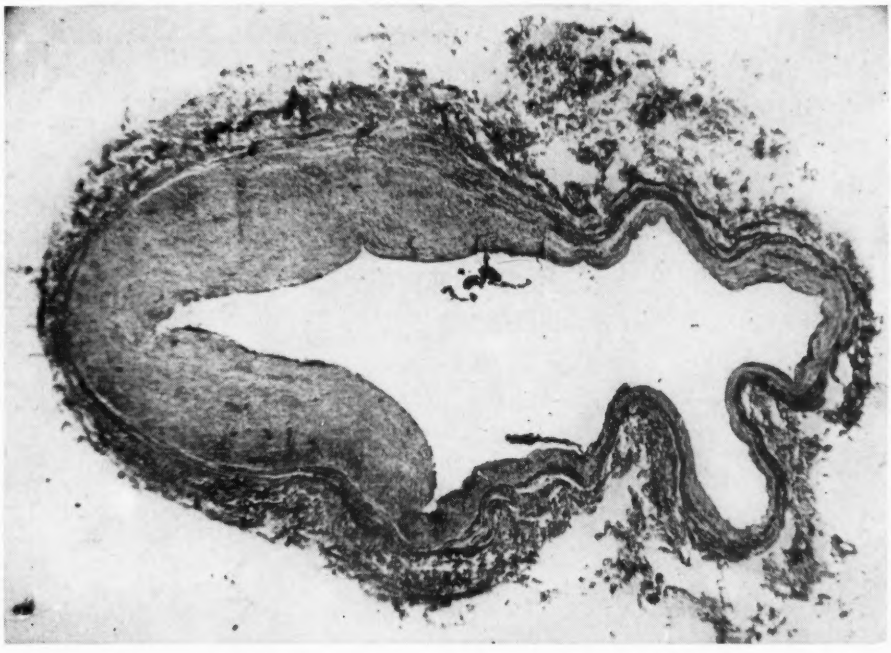

Fig. 2.—Cross section of same vein just above the knee. Note the marked eccentric thickening of vein wall due to organization of pre-existing thrombus.

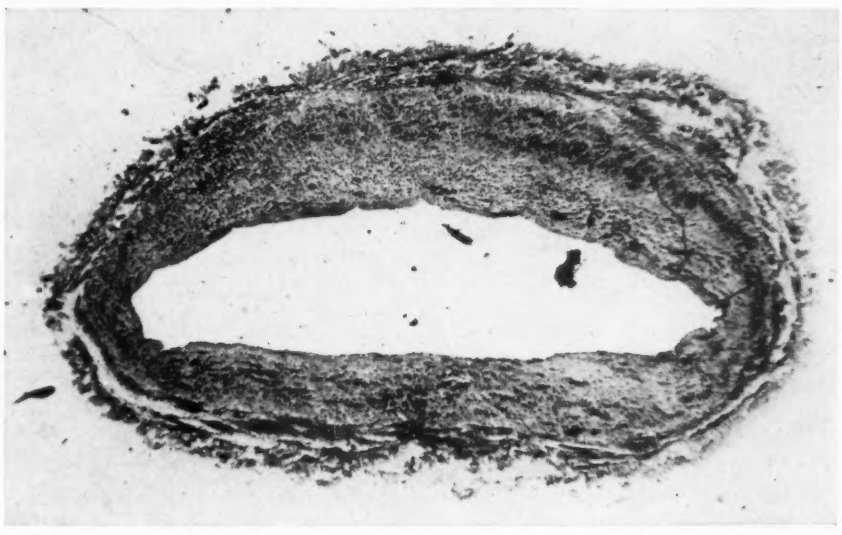

Fig. 3.—Cross section of same saphenous vein below the knee. Note the evidence of previous sclerosis with organization and almost complete restoration of patency of vein. This has occurred in the past four years.

The saphenous vein, many times, is more difficult to locate above the knee than in the femoral triangle (Scarpa) (Fig. 4, *A*), especially in obese individuals. To overcome this difficulty the idea was conceived of inserting a malleable intraluminal guide into the distal segment of the vein near the fossae ovalis (Fig. 4, *C*). A ligature is placed around the distal end and held tight to prevent the reflux of blood while the guide is being inserted (Fig. 4, *C*). The

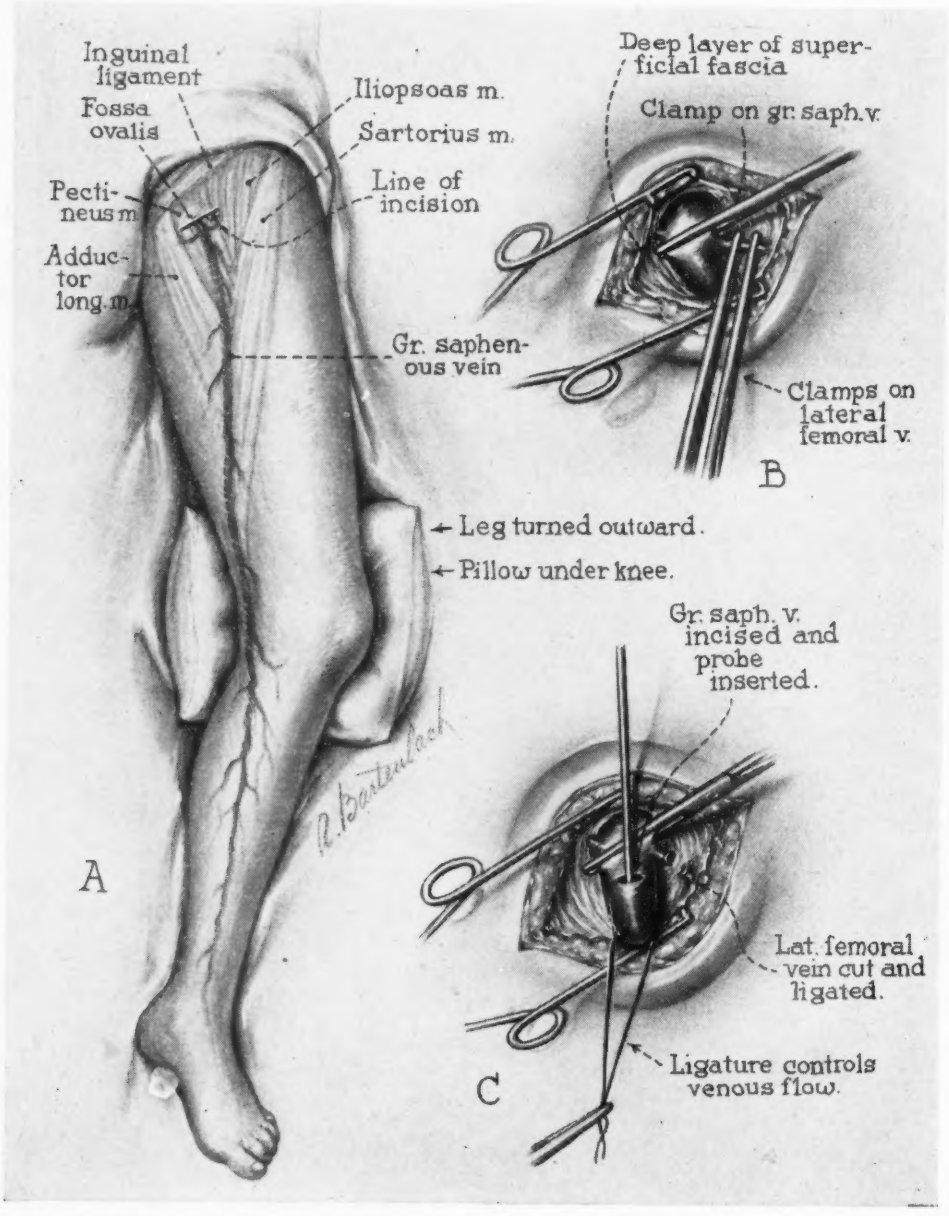

Fig. 4.—Diagram showing (*A*) location of fossae ovalis in apex of femoral triangle and course of saphenous vein down the leg, (*B*) lateral femoral cutaneous vein being clamped, (*C*) malleable intraluminal guide being inserted into vein near fossae ovalis.

guide follows the lumen of the vein and can easily be palpated through the subcutaneous tissue. An incision is made over the guide in mid-thigh and the vein easily exposed and dissected out (Fig. 5, *A* and *B*). The proximal end is doubly ligated (Fig. 5, *C* and *D*), a segment removed, and the guide withdrawn. The distal end is clamped with a hemostat since the guide will be inserted into the distal end later (Fig. 8, *A*).

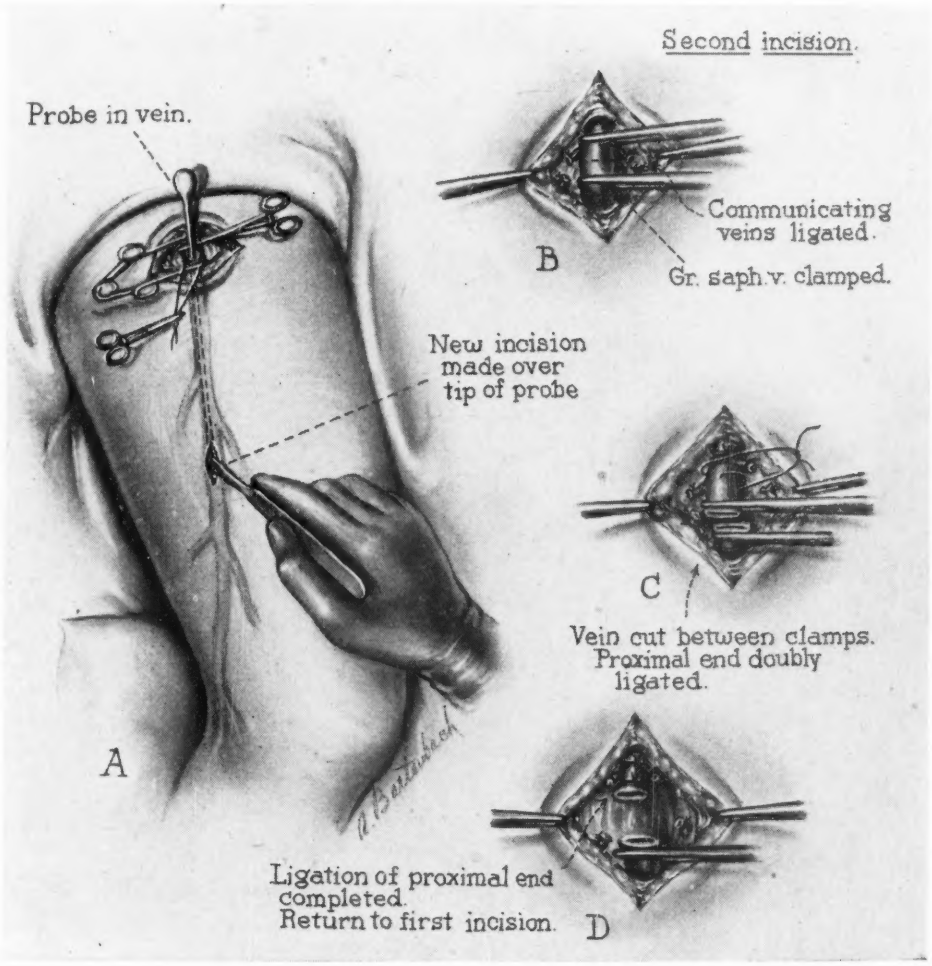

Fig. 5.—Diagram showing (*A*) an incision being made in mid-thigh over the guide; (*B*) vein dissected out and communicating vein, dissected and ligated; (*C*) and (*D*) double ligation of proximal end of vein.

Many times a communicating vein (Fig. 5, *B*) is isolated and ligated. An aneurysm may be found opposite the entrance of an incompetent communicating vein (Fig. 7). Sometimes the guide enters one of these aneurysms or a communicating vein (Fig. 7). This aids in locating a communicating vein. When the communicating vein is dissected out, the guide can be pulled out a short distance and reinserted into the lumen of the saphenous after the communicating vein or aneurysm has been isolated.

The guide is withdrawn after the proximal ligation in mid-thigh has been completed. The distal end of the saphenous in the femoral triangle is doubly ligated, one ligature being transfixed (Fig. 6, *A*). Cotton, No. 30 for the larger veins and No. 40 for the smaller vessels, is used throughout the operation, except for the skin where interrupted dermal is used.

The lateral femoral cutaneous (Fig. 4, *B* and *C*) and medial femoral cutaneous veins if present may be ligated and cut at this time if this was not done previous to inserting the intraluminal guide. Likewise the superficial external

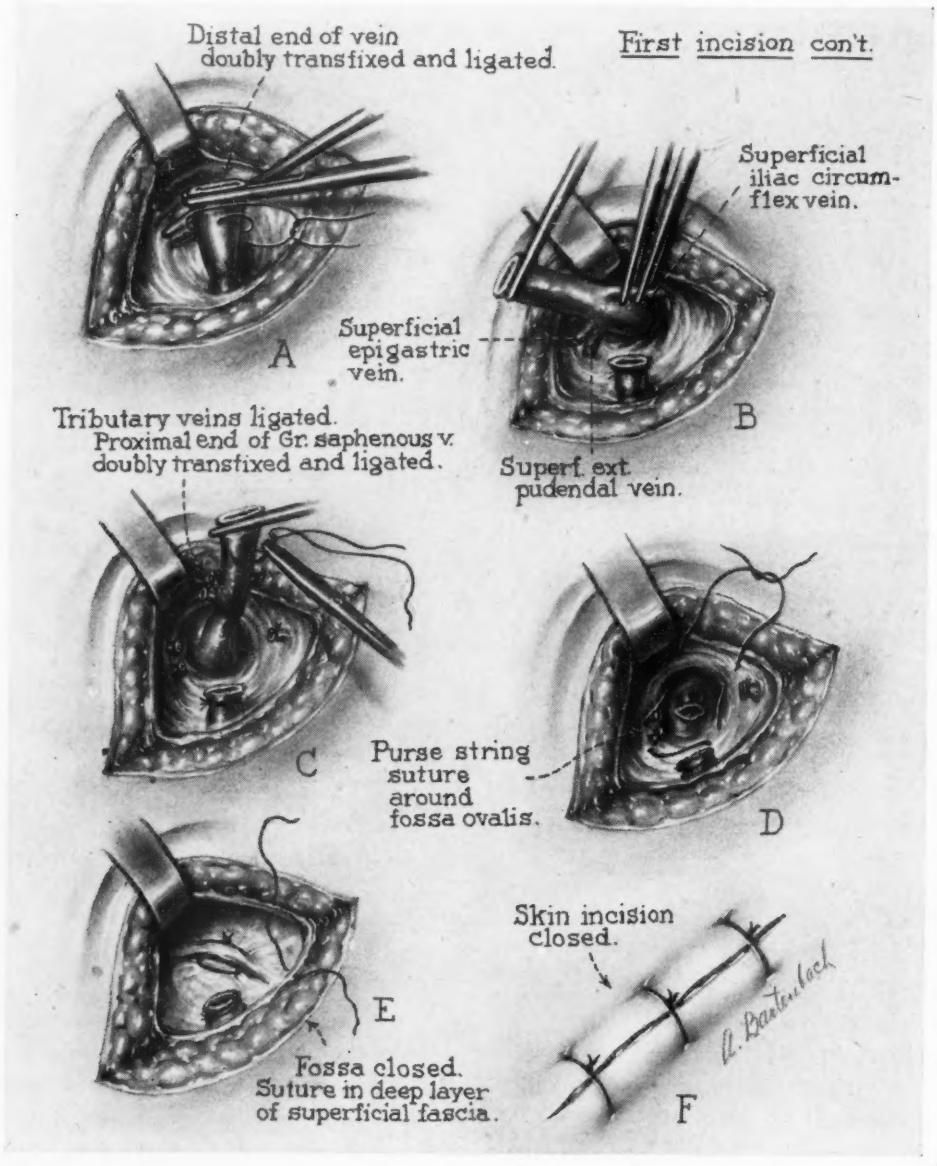

Fig. 6.—Diagram showing fossae ovalis and branches usually found in this area.

pudendal vein or veins, since usually there are more than one (Fig. 6, *B*), the superficial circumflex iliac (Fig. 6, *B*), and the superficial epigastric (Fig. 6, *B*) are ligated and cut.

The saphenous vein is dissected at the fossae ovalis down to its entrance into the femoral. This dissection as well as all blood vessel dissections is facilitated by using a small piece of umbilical tape rolled up and clamped to the end of a hemostat (Fig. 9). It is then doubly ligated snug to the femoral vein, one ligature being transfixed and the segment of vein cut and removed (Fig. 6, *C*).

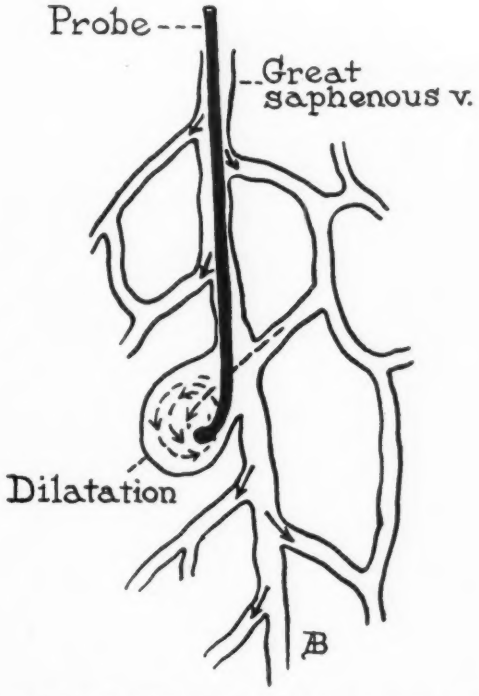

Fig. 7.—Diagram showing how guide may locate an aneurysm or communicating vein.

The fossae ovalis is closed with a purse-string suture (Fig. 6, *D*). The deep layer of the superficial fascia is approximated (Fig. 6, *E*) and the skin closed with interrupted dermal (Fig. 6, *F*).

Next a return is made to the mid-thigh incision (Fig. 8). The intraluminal guide is again inserted into the distal end of the vein, palpated above the knee, and the vein easily located, exposed, dissected out, and a segment removed and ligated (Fig. 8, *A*). Again the guide is withdrawn and the distal end of the vein in the mid-thigh incision ligated. The proximal end of the vein at the knee incision is ligated, but the distal end clamped as before.

The guide is next inserted down the vein from the knee incision to below the knee where the vein is again palpated over the guide, exposed, dissected out, ligated, and resected as before. This can be repeated to near the termination of the saphenous vein (Fig. 8, *B*).

The dilated veins seen below the knee when standing usually prove to be branches of the main vein. The guide may enter this superficial communication but can be withdrawn a short distance, manipulated, and then enter the main vein which arises near the medial malleolus. This has been demonstrated numerous times.

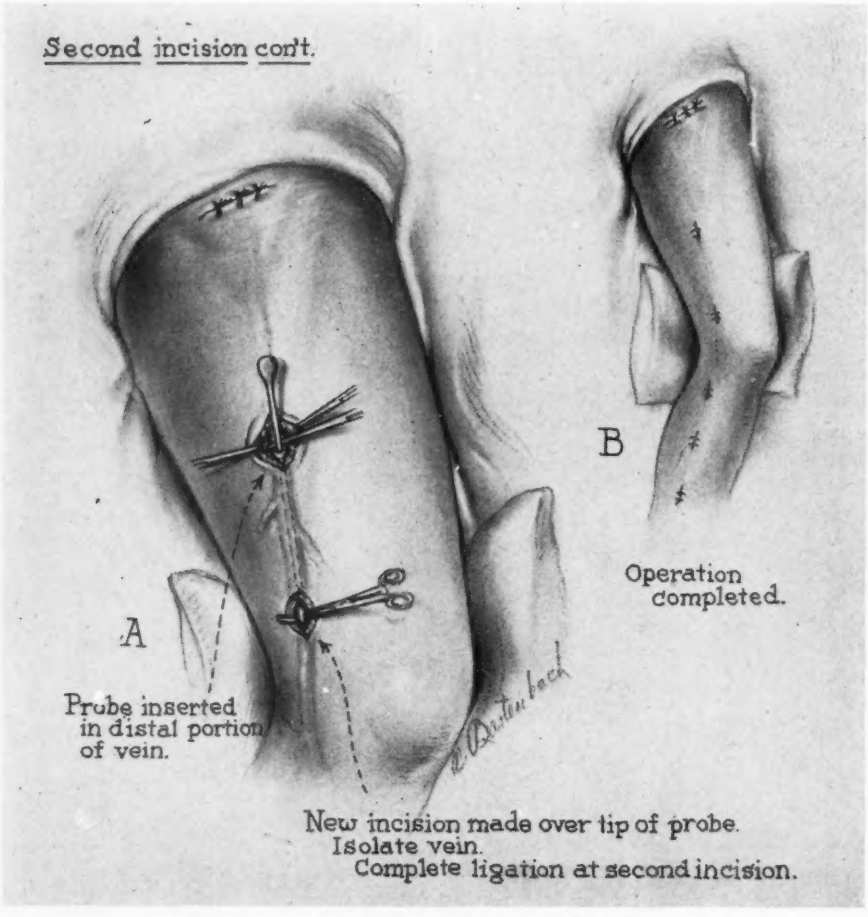

Fig. 8.—Diagram showing (*A*) the guide being inserted at the mid-thigh incision, into the distal end of the vein. The vein is again isolated just above the knee with the aid of the intraluminal guide. (*B*) Showing end result of retrograde ligations and phlebectomy above and below the knee.

The malleable intraluminal guide may be used further by exposing and opening the saphenous vein above or below the knee and directing it upward. This maneuver aids in determining whether the saphenous was properly ligated previously at the fossae ovalis. If not, a religation and excision are indicated. It further aids in determining the extent, if any, of the sclerosis.

Longitudinal incisions, in my experience, heal better than transverse ones and give a better cosmetic result. So far none of the patients have complained of the resulting scar, which in most instances is minimal and hardly visible after a few years.

An elastic adhesive bandage or Unna's boot, if a varicose ulcer is present, is applied from the toes to the knee. The patient is ambulatory two hours after operation. The stitches are removed in one week. The incisions usually heal by first intention and infection is rare.

Recurrences may and do occur with this procedure but in my experience not as frequently as when retrograde injection is used. If recurrences do occur it is by the formation of new collaterals rather than by organization of a thrombus alone. A thrombus will organize more quickly and frequently than collaterals will form. If recurrences do occur they can be treated by injection of the collaterals when they appear or by further ligation.

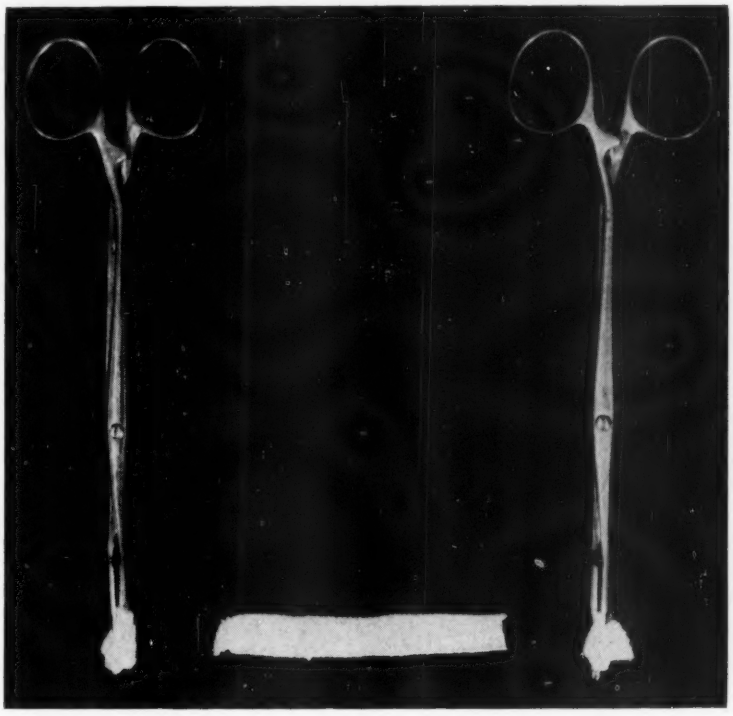

Fig. 9.—Photograph showing piece of umbilical tape rolled up and attached to the end of a hemostat. This provides dry gauze dissection without bulk which is encountered when large dry sponges are used. This aids in dissection of veins.

McPheeters* has wisely stated that patients who are prone to develop varicose veins should consult their physician at regular intervals for inspection and injection of any new varicosities, just as they should visit their dentist for inspection and care of their teeth.

This procedure is presented not as a cure-all for varicose veins, but as a method of procedure which has helped in the surgical treatment of varicose veins. The procedure is thought to be surgically sound and it is hoped that others may profit by this report.

*McPheeters, H. O.: Surg., Gynec. & Obst. 81: 355-364, 1945.

SUMMARY

1. Varicose veins may recur following high saphenous ligation combined with retrograde injection. This recurrence may follow inadequate surgery in the femoral triangle resulting in a reverse flow of blood upon the thrombus, which in turn may become recanalized.

2. Varicose veins may recur following adequate surgery in the femoral triangle combined with retrograde injections. This recurrence may be due to incompetent communicating or perforating veins, which hastens recanalization of the thrombus in the saphenous.

3. A thrombosed vein has a tendency to recanalize itself.

4. Retrograde ligation and excision of segments of the saphenous vein at different levels above and below the knee should interrupt any reverse flow of blood which might come from incompetent communicating or perforating veins higher up.

5. Retrograde ligation and excision in my opinion are superior to retrograde injection.

6. A medium-sized malleable intraluminal guide facilitates finding the saphenous vein both above and below the knee, and many times in locating an incompetent communicating or perforating vein or aneurysm.

7. Cotton is a good suture material, as there is little or no tissue reaction following its use.

8. A small piece of umbilical tape rolled upon itself and attached to a hemostat facilitates dissection of the vein.

9. Longitudinal incisions are superior to transverse incisions in retrograde saphenous ligation and phlebectomy.

GRADED LEG EXERCISES

JOSEPH K. NARAT, M.D., AND ARTHUR F. CIPOLLA, M.D., CHICAGO, ILL.

UNTIL the problem of a successful therapy of pulmonary embolism has been solved, all efforts must be concentrated on its prevention.

Collins[1] tabulated the incidence of pulmonary embolism as reported in the literature during the preceding twenty-four years by fifteen authors. In 316,060 cases the incidence was determined to be 0.52 per cent. In 172,888 operations of all types performed at the Mayo Clinic[2] there were 343 fatal emboli, indicating an incidence of 0.2 per cent of 1 in 500 cases. Pulmonary embolism accounted for 5.9 per cent of all postoperative deaths. A survey of large collective statistics by de Takats and Jesser[3] revealed a fairly steady incidence in large services, namely, from 0.1 to 0.2 per cent of all operations, 2 per cent of all deaths, and 6 per cent of postoperative deaths. Erskine and Shires[4] found that the mortality from pulmonary embolism after abdominal operations performed at the Chelsea Hospital for Women was 0.415 per cent or 1 fatal embolism in 240.5 operations.

The frequency of pulmonary embolism in obstetrics is similar to that following surgery. Nettleblad[5] reported 0.86 per cent of thrombosis and embolism in 50,000 deliveries.

It can be seen from the previously mentioned statistical data that the incidence of postoperative or post-partum pulmonary embolism is too small to warrant the routine employment of prophylactic measures. This applies especially to those which require supervision of the nursing personnel and thus consume their valuable time. On the other hand, no effort should be spared to prevent occurrence of this tragedy in cases where such a complication may be expected. Patients with hypotension, cardiac diseases, varicosities of lower extremities, abdominal distention, obese individuals, patients over 50 years of age, those with a past history of a peripheral vascular disease or blood dyscrasia as well as those who are convalescing from an extensive or technically difficult pelvic laparotomy are prospective victims of a venous thromboembolic disease. It is in this group of patients that the following prophylactic measures are in order: (1) leg exercises to prevent stagnation of the blood column, (2) no tight binders which form a mechanical obstruction to the venous backflow, (3) Trendelenburg position to facilitate the return of venous blood from the lower extremities by the effect of gravity,[3, 6] (4) avoidance of Fowler's position which causes stasis in the lower legs because of their pendancy and the compression or kinking of the popliteal veins,[7] (5) encouragement of deep respirations essential for propulsion of blood, (6) early ambulation, (7) early administration of fluids to counteract dehydration with resulting hemoconcentration, (8) dietary regime[8] (low fat, low protein diet as the least conducive to thrombotic changes), (9) frequent change of position, (10) employment of dicumarol or heparin in selected cases.

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The discussion of all these and other measures is beyond the scope of this paper. There is a general agreement that two measures deserve the greatest attention in the prophylaxis of pulmonary embolism: (1) leg exercises and (2) use of heparin and dicumarol in selected cases.

Stagnation of venous blood is one of the most readily controllable factors in postoperative thrombosis. In view of the fact that the most common source of thrombosis leading to embolism is the femoral vein and its tributaries, the lower extremities are receiving the greatest attention in attempts to maintain the muscle tone and to promote the flow of venous blood. For this purpose Pool[9] suggested a set of active exercises and early ambulation. Various devices have been developed for active and passive exercises; rollers against which the patient is instructed to rub his feet and legs,[10] rhythmically contracting air cushions strapped to the patient's legs,[11] levers raising and lowering the patient's limbs,[11] pedaling apparatus,[12, 13] a device consisting of a stand which carries two pulleys with counterbalance weights,[14] oscillating bed,[15] an apparatus operated by patient's hands.[16]

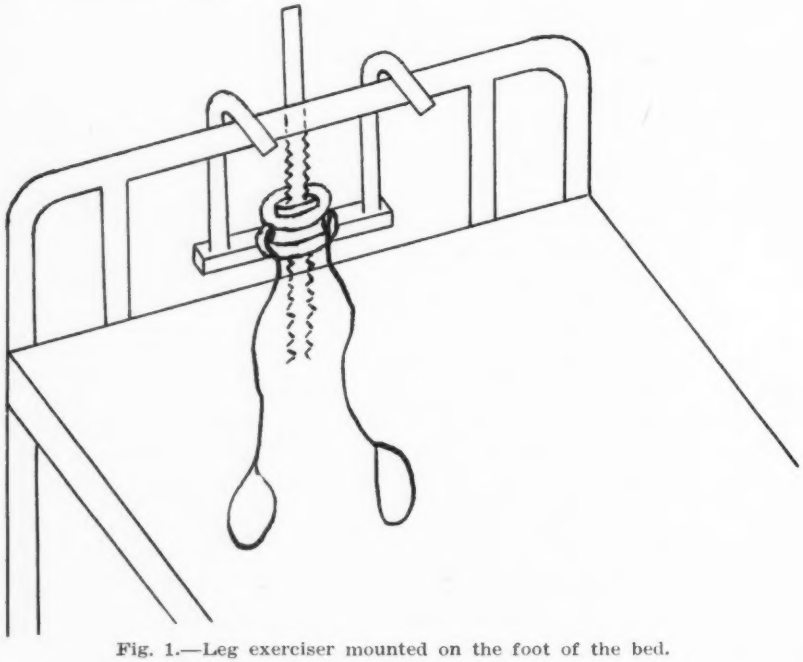

Fig. 1.—Leg exerciser mounted on the foot of the bed.

The efficiency of postoperative exercises in prevention of pulmonary embolism is attested by Erskine and Shires[4] who reported that the incidence of fatal embolism after abdominal operations was reduced by more than one-half following introduction of postoperative exercises and massage. Shaw and Rickards[10] found fatal embolism to be five times more common in a hospital where exercises are not included in the postoperative treatment as compared with another institution where exercises are carried out as a routine.

While the value of leg exercises has thus been established, certain disadvantages of the devices now in use must be mentioned: most of them are bulky

and either take considerable space in the bed, interfering with the patient's comfort, or protrude from the bed, blocking the free passage in the room; patients must be uncovered to perform the exercises; some devices are impractical or expensive or both; they are time consuming because they require supervision; finally, they provide no facilities for registration which is essential because pain, lack of interest, or lassitude caused by sedation may prevent the patient from faithfully carrying out the prescribed order.

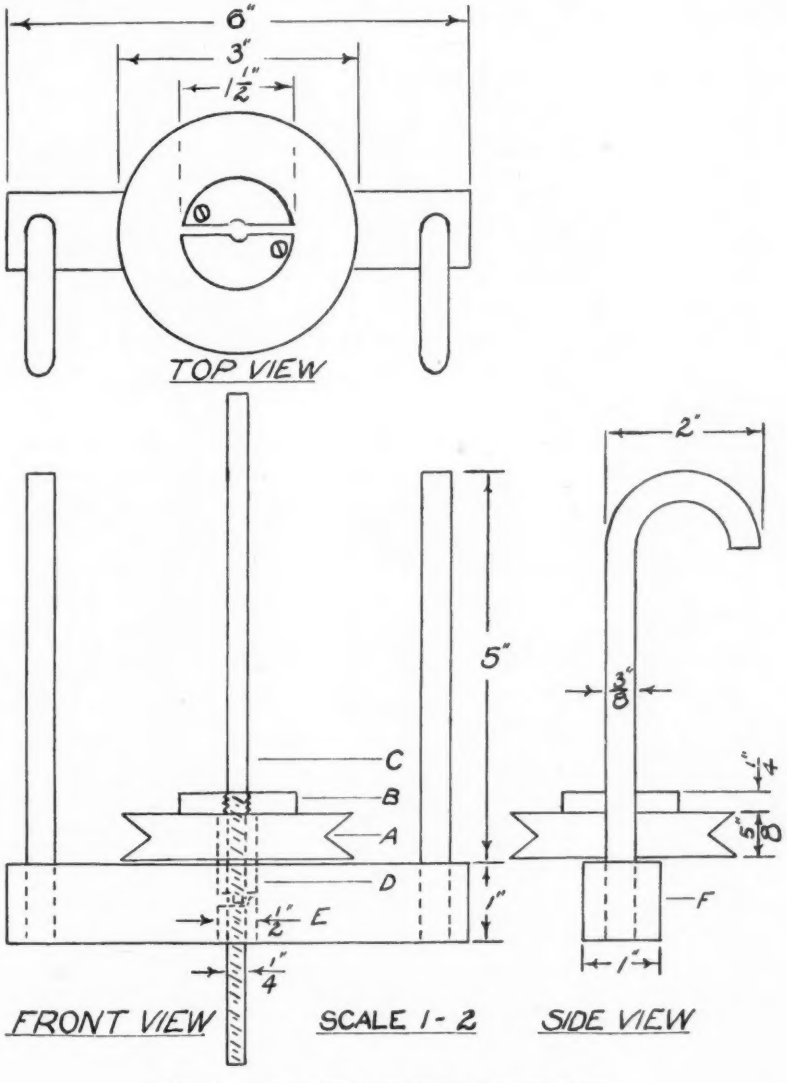

Fig. 2.—Mechanical drawing of leg exerciser.

To overcome such shortcomings, we developed a leg exerciser[17] which is relatively low in cost, has a simple construction, requires very little space, does not require uncovering the patient, and registers the number of exercises. The apparatus consists essentially of a pulley which rotates whenever a cord placed

around it is pulled by the patient's feet. A vertical rod attached to the pulley trips the arm of a counting machine. This device saves valuable time of the nursing personnel because no supervision is required; a glance at the counting chamber shows whether the patient carried out the exercises as directed.

In an attempt to simplify the device further and to make it still less expensive and more sturdy, we developed a new apparatus for calisthenic exercises of lower extremities.

The main parts of the apparatus are a pulley and a vertical threaded rod mounted on a crossbar and attached to the foot of the bed with two hooks. The pulley is equipped with a cord whose ends are attached to the patient's feet or ankles. When the patient alternately flexes his knees, the pulley rotates, causing the vertical shaft to rise. As the rod is marked with numerals, it is easy to check whether the patient performed the number of exercises prescribed.

TECHNICAL DETAILS

A pulley (*A*) 3 inches in diameter with a ½ inch hole carries a disk (*B*) ¼ inch thick and ½ inch in diameter. The disk is tapped with a No. 14-28 S. A. E. thread and is split in the vertical plane. The disk is attached to the top of the pulley with two screws. A 14-28 S. A. E. threaded rod (*C*) rides the center of the threaded disk. The rod is ground 1/16 inch on one side throughout its entire length. The center of the pulley is equipped with a bushing (*D*) ½ inch in diameter, with a ¼ inch central hole; at the bottom end of the upper bushing there are two ⅛ by ⅛ inch prongs which fit a lower bushing (*E*) containing two spiral grooves to fit the prongs in the form of a ratchet. This ratchet allows the upper bushing to move in one direction only. The upper bushing is fixed to the pulley while the lower is attached to the cross-bar (*F*) 1 by 1 by 6 inches. The lower bushing contains a hole through which an 8-32 standard screw is inserted. This screw rides the ground surface of the vertical rod.

SUMMARY

A new apparatus for leg exercises has a very simple construction, is inexpensive, occupies practically no space, does not require uncovering the patient, and registers the number of exercises.

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SUCCESSFUL PRIMARY REPAIR OF LACERATED STENSON'S DUCT

RALPH E. GOODALL, M.D., AND SARAH E. FLANDERS, M.D., NEW YORK, N. Y.
(From the Second [Cornell] Surgical Division of Bellevue Hospital)

THE anatomic location of Stenson's duct makes it subject to injury in deep wounds of the cheek. As failure to repair the duct results in a salivary fistula with its distressing symptoms, it is imperative to attempt to reapproximate the divided ends at the time of initial débridement. Eight cases of primary suture of Stenson's duct have been recorded in the literature and the method used varied but slightly in each instance. Success of the procedure seems to have depended on the use of an inlying dowel firmly fixed in place at the time of early débridement and on the anatomic structure of the duct which makes it suitable for suture. It is our purpose, after a brief review of the anatomy, to report another case of primary suture of the parotid duct and to show the success of the procedure by accompanying pictures of the patient and sialograms taken six months following operation.

ANATOMY

The parotid duct measures two and one-half inches in length. Its surface anatomy corresponds to a line drawn across the face about one fingerbreadth below the zygoma running from the tragus to a point midway between the vermilion border of the upper lip and the ala of the nose. In its course it crosses over the masseter muscle at the anterior border of which it dips down into the substance of the upper part of the buccinator muscle, which it pierces, and then runs obliquely forward for a short distance between the buccinator muscle and the oral mucous membrane. The opening on the inner surface of the cheek is through an orifice opposite the second upper molar tooth. The wall of the duct is dense and of considerable thickness, consisting of an external fibrous coat containing contractile muscle fibers and an internal mucous coat lined with short columnar epithelium.

CASE REPORT

E. M., a 35-year-old white man, was admitted to Bellevue Hospital on Dec. 31, 1944, with multiple lacerations of the face and hands, having been assaulted with a sharp instrument about one hour prior to admission. On physical examination the patient was conscious but with a strongly alcoholic odor to the breath. There was a deep laceration, 6 cm. in length, extending obliquely from over the zygoma at a point about 3 cm. anterior to the tragus of the left ear almost to the midpoint of the body of the mandible. The buccal mucosa was intact. He was unable to move the left side of the face. There was also a 2 cm. laceration just over the lateral margin of the left eyebrow and a 2 cm. laceration at the base of the nose extending just above the left eyebrow. A 6 cm. laceration extended across the knuckles of the third to the fifth fingers of the left hand with division of the tendons where the assaulting instrument had penetrated directly into the bony substance partly severing the metacarpal heads. He had a flexion deformity of the third to the fifth fingers due to a pre-existing Dupuytren's contracture. A similar deformity involved the fifth

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finger of the right hand and there was a superficial laceration of the right thumb. The rest of the physical examination was within normal limits except for an old upper right rectus scar.

Two hours after admission a débridement and suture of the multiple lacerations were performed under sodium pentothal anesthesia. All wounds were uncomplicated except for the one in front of the left ear where exploration revealed complete division of Stenson's duct in the masseteric portion and division of three terminal branches of the facial nerve. The wound was cleansed with green soap and peroxide and irrigated with approximately 6 L. of physiologic saline solution over a period of twenty minutes. All devitalized tissue was removed. The masseter muscle was sutured with 000 plain catgut. An attempt was made to approximate the severed ends of the facial nerve branches but the small caliber of the nerves made accurate approximation doubtful. The proximal end of the severed

Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—Healed laceration at six months.
Fig. 2.—Facial paralysis resulting from division of branches of facial nerve.
Fig. 3.—Facial paralysis.

duct was easily identified. The distal end was located by passing a small ureteral catheter through the orifice in the mouth. When the catheter emerged in the laceration, it was passed into the proximal segment of the duct. The two ends were then sutured over the catheter, using interrupted sutures of fine black silk. Primary closure of the wound was effected by approximation of subcutaneous tissues with interrupted sutures of 000 plain catgut and of the skin edges with verticle mattress sutures of black silk. The catheter was taped securely to the lower lip to hold it in place, and a dry sterile dressing was applied. A tenorrhaphy was performed on the left hand.

Postoperatively the patient was given nothing by mouth, and oral hygiene was maintained by mouth care every two hours. He had a slight temperature elevation for four days, spiking to 103° F. on the fifth and sixth days, with subsequent return to normal. On the fourth postoperative day there was slight swelling over the left parotid gland. The wound, however, was clean and the skin silks were removed. There was slight reaction about the orifice of the duct in the mouth. No flow of saliva was noted. The catheter was removed on the fifth postoperative day. The patient was fed parenterally until the sixth day when he was placed on a full fluid diet. Change to a soft diet on the seventh postoperative day was tolerated well by the patient, with no swelling or pain in the region of the left parotid gland, and a free flow of saliva was noted from the stoma of Stenson's duct. Be-

cause of the left facial paralysis, the eye department performed a tarsorrhaphy on the twelfth postoperative day. This was unsuccessful. He was discharged from the hospital on the eighteenth postoperative day. He was contacted six months later, at which time the pictures (Figs. 1, 2, and 3) and the sialograms (Figs. 4 and 5) were taken. There was no fistula, no swelling, and no tenderness of the parotid gland, and the sialograms showed a normal pattern with no stenosis of the duct.

Fig. 4.

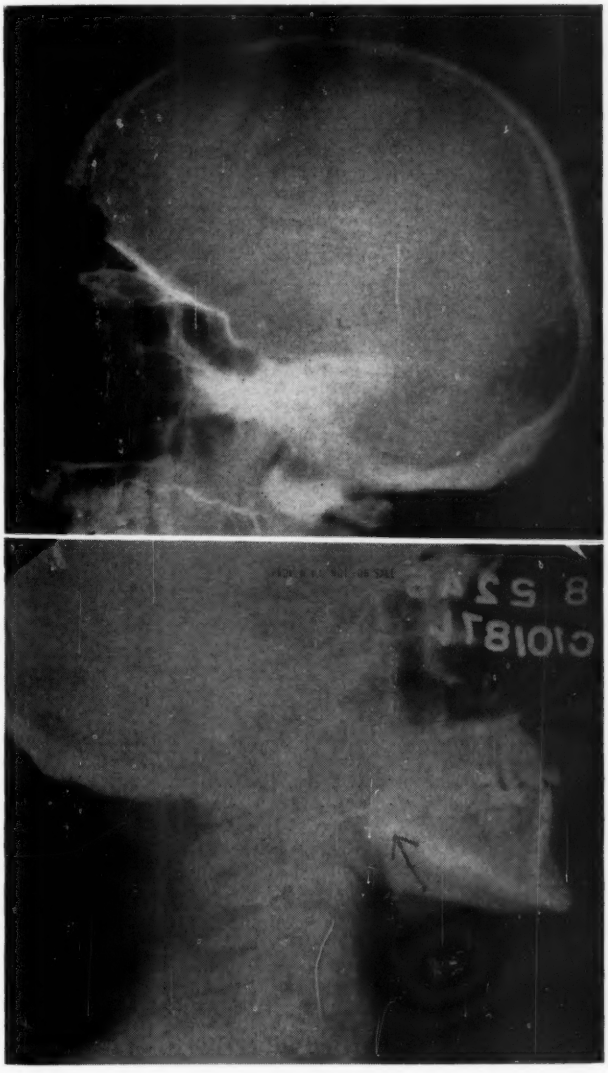

Fig. 5.

Fig. 4.—Sialogram six months postoperative.
Fig. 5.—Sialogram six months postoperative.

DISCUSSION

Even though the reported cases show a variance in the form of treatment, certain constant factors are found: Débridement and suture were carried out

as soon as possible after injury to insure a clean wound, and an inlying dowel was used in every case except one.[4] The type of dowel varied (see Table I).

TABLE I. PERTINENT FACTS CONCERNING USE OF DOWELS

AUTHOR	DOWEL	SUTURES	HOW DOWEL SECURED	DRAINAGE	TIME LEFT IN	TIME REPAIR AFTER INJURY
Tees	Stiff iodine catgut	Fine gut	Gut projected into mouth	No	?	4 hr.
Dickinson	Silkworm gut	00 chromic gut	Fixed by suture to point exit in mouth	Yes	2 days	30 min.
Black and Flagge	Ureteral catheter	0 chromic gut	Sutured to buccal mucosa	No	9 days	?
Hill	None	00 plain		Yes	?	?
Brohn and Bird	Fusiform bougie	Silk	Exit through upper lip	No	7 days	Stat.
Christofferson et al.	Horsehair suture	Silk	Taped to skin	No	7 days	5½ hr.
Wallace	Silkworm gut	Cotton	Sutured to buccal mucosa	No	7 days	Stat.

Tees[1] used stiff iodine catgut No. 1, Dickinson[2] silkworm gut, Black and Flagge[3] an ureteral catheter, Brohn and Bird[5] a fusiform bougie, Christofferson and associates[6] a horsehair suture, and Wallace[7] silkworm gut. Successful results were obtained in each instance, suggesting that the type of dowel is not as important as the fact that a dowell is used to maintain, but not to occlude completely, the lumen of the duct during suturing and until healing has occurred. In addition, the anatomic structure of the duct probably contributes to success as its thickness allows the accurate and substantial placement of the sutures. The dowels have been left in place for from two[2] to nine[3] days. Probably the most difficult problem is how to secure the dowel in place so that it will not slip out before the tissues have healed. The dowel has been anchored to the buccal mucosa by suture,[2, 3, 7] passed through the upper lip,[5] or taped with adhesive to the angle of the mouth.[6] In the repair of the duct the suture material varied, gut,[1, 2, 4, 8] silk,[5, 6] and cotton[7] having all been used with equally good results. The wounds have been closed without drainage in all instances but two,[2, 5] when a drain was used.

It then appears that salivary fistula can be prevented by successful primary suture of Stenson's duct. This can be accomplished by early débridement, suturing the severed ends over an inlying dowel which is maintained in position by firm fixation to a neighboring structure, and primary closure of the wound. Adequate oral hygiene probably contributes to a satisfactory outcome.

SUMMARY

A case of successful primary suture of Stenson's duct with a review of the anatomy has been recorded. The operation was performed within three hours of injury. After careful débridement of the wound an ureteral catheter was

passed through the duct as an inlying dowel, and silk was used to approximate the ends of the duct. Fixation of the dowel in place was accomplished by taping to the lower lip. The patient had a satisfactory postoperative course. When seen six months later he had no symptoms referable to the parotid gland and a sialogram showed no abnormalities of the duct.

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THE USE OF PENICILLIN IN CONNECTION WITH THE GRAFTING OF BONE INTO INFECTED DEFECTS IN THE SKULLS OF EXPERIMENTAL ANIMALS

H. J. McCorkle, M.D., Edwin Kerr, M.D., Sanford Rothenberg, M.D., and Helen Warmer, A.B., San Francisco, Calif.

(From the Division of Experimental Surgery of the University of California Medical School)

INFECTED bone defects were produced in the skulls of dogs by excising segments of bone, crushing the temporal muscles, contaminating the wounds with street dirt, and closing them with sutures (Fig. 1). After the acute phase of the infections subsided, chronic granulating wounds and sinuses remained. A considerable number of trial experiments were performed before suitable uniform chronic infected skull defects were produced by this method. Twenty dogs with well-established infections were selected for the main experiments. Bacteriologic cultures were made from the wounds and from the infected tissues removed surgically, and penicillin-sensitivity studies were carried out. In Table I are listed the bacteria cultured from the infected wounds of the twenty animals before the bone grafting procedures.

After the chronic infections had become well established, the animals were subjected to operations, at which granulations, scar, and sequestra were removed, bone grafts placed in the skull defects (and retained in position with fine steel wires placed through small drill holes), and the wounds closed in layers with cotton sutures without drainage (Fig. 2). In one-half of the animals cortical bone grafts were used, and in the others cancellous bone was used for the grafts. Ten animals (five cortical grafts and five cancellous grafts) were used as controls, and the other ten (five cortical and five cancellous grafts) were given 100,000 units of penicillin daily for two days preoperatively and for twenty-one days postoperatively. Penicillin was given by intramuscular injection at four-hour intervals.

The soft tissue wounds of eight of the ten animals treated with penicillin healed without infection. Trivial infections appeared in two of the penicillin-treated animals; one of these developed a hematoma infected with *P. vulgaris;* the other healed per primam, but five weeks postoperatively developed a small draining sinus, from which penicillin-sensitive organisms were cultured (this healed with additional penicillin therapy). The wounds of nine of the ten untreated control animals broke down with acute gross infection within the first few postoperative days; the remaining control animal developed multiple suture hole abscesses and slight drainage from the anterior aspect of the incision. Signs of illness from general sepsis were obviously present in all untreated control animals; they appeared thin and lethargic, and ate poorly. All

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of the ten penicillin-treated animals were entirely free of signs of toxicity from sepsis, were alert and active, and had good appetites. In Table II are summarized the manifestations of infection in these twenty experimental animals.

One of the penicillin-treated animals died thirty-nine days postoperatively, from causes beyond the control of the experimenters, but the other nine survived with well-healed wounds for the remainder of the six-month postoperative experimental period. In the control group the wounds of two of the animals suppurated for one to two months postoperatively, those of seven animals sup-

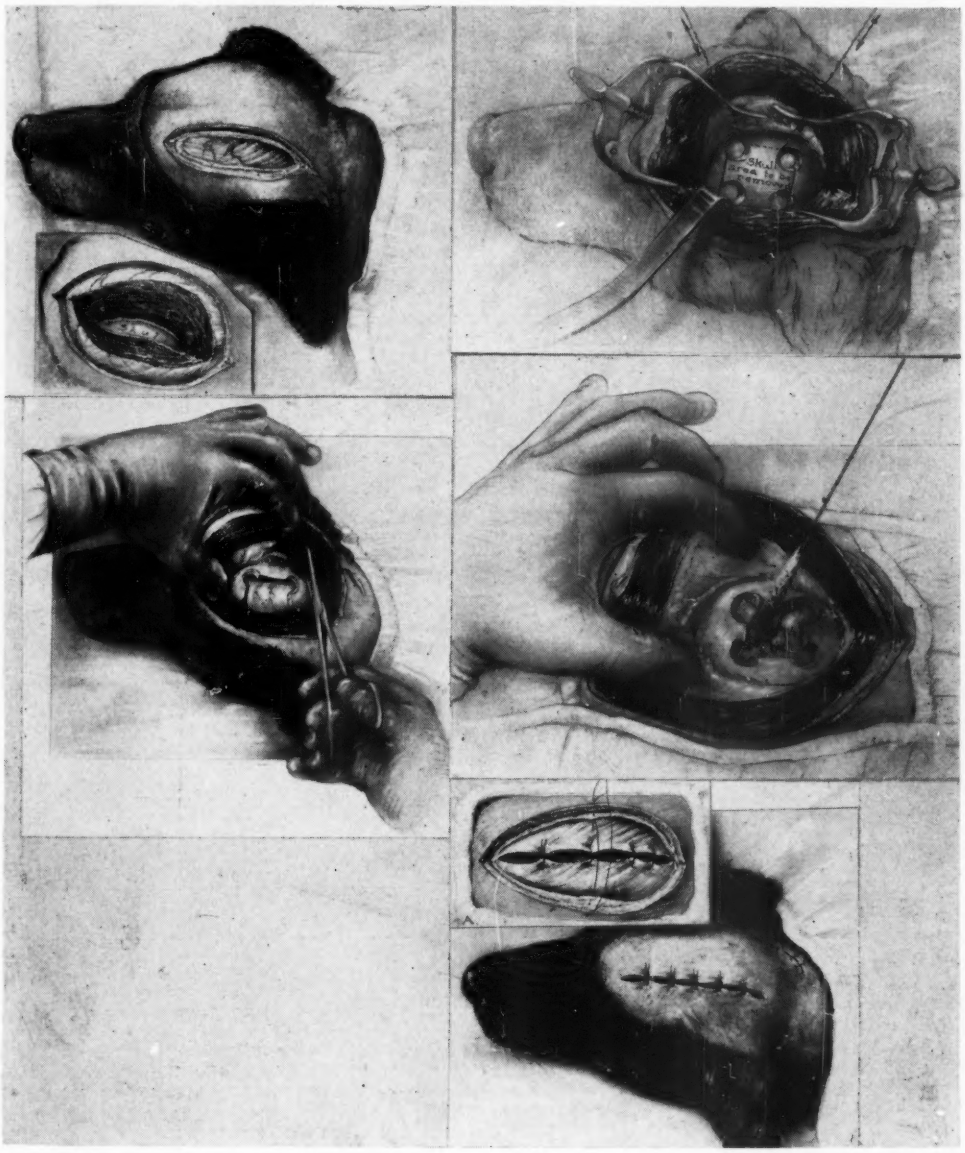

Fig. 1.—Diagrams indicating method for producing experimental infected skull defects in animals.

TABLE I

ORGANISM	NUMBER OF ANIMALS	PENICILLIN SENSITIVE	PENICILLIN RESISTANT
Beta hemolytic Streptococcus	14	13	1
Alpha hemolytic Streptococcus	2	1	1
Gamma Streptococcus	9	1	8
Hemolytic *Staphylococcus aureus*	11	11	0
Hemolytic *Staphylococcus albus*	8	8	0
Nonhemolytic *Staphylococcus aureus*	3	3	0
Nonhemolytic *Staphylococcus albus*	3	2	1
Clostridia	18	18	0
Escherichia coli	8	0	8
Aerobacter aerogenes	3	0	3
Bacillus pyocyaneus	1	0	1
Proteus vulgaris	2	0	2
Diphtheroid bacilli	7	0	7
Bacteroides	2	—	—

TABLE II

	ILLNESS FROM SEPSIS	HEALING OF SOFT TISSUE WOUNDS		
		WITHOUT INFECTION	TRIVIAL INFECTION	GROSS INFECTION
Penicillin treated	0	8	2	0
Controls	10	0	1	9

purated for two to three months after operation, and the wound of one animal suppurated for the entire six-month postoperative experimental period.

X-ray examinations of the bone-grafted areas were made at appropriate intervals during the postoperative period. The x-ray views in the group of animals treated with penicillin in the early postoperative period revealed sharply outlined grafts that remained unchanged in size or position, and without evidence of absorption of the grafted bone (except for one small area near a drill hole in one graft, which probably was caused by compression due to a tight wire). X-ray evidence of bony union between the graft and the skull appeared between the fifth and twentieth postoperative weeks in eight of the nine penicillin-treated animals. The x-ray evidence of bone repair did not differ significantly

TABLE III

	NUMBER OF ANIMALS	X-RAY APPEARANCE OF BONE GRAFT				
		APPARENTLY VIABLE	ABSORBED	COMPLETE SEQUESTRATION	EXTRUSION	BONY UNION
Penicillin treated	9	9	0	0	0	8
Controls	10	2	5	1	2	2

TABLE IV

	NUMBER OF ANIMALS	VIABLE GRAFTS	EXTRUSION—SCAR REPLACEMENT	ABSORPTION—REPLACEMENT WITH SCAR	SEQUESTRATION OF GRAFT	BONY UNION
Penicillin treated	9	9	0	0	0	8
Controls	10	2	2	5*	1	2

*In two of these animals very small residual pieces of the original bone grafts were imbedded in extensive scar.

in the cortical and cancellous grafts. The x-ray studies in the untreated control animals indicated evidence of decrease in size and extensive absorption of the grafts in eight out of ten animals. In these eight animals, five of the grafts were partially or completely absorbed, two were extruded through the open infected wounds, and one remained in place without attachment, as a sequestrum. In the other two control animals, one had x-ray evidence of apparent viability and bony union between graft and skull; the other had x-ray evidence of decreased size and density from absorption, but later regained its normal density and also developed x-ray signs of bony union between two sides of the graft and the skull defect. In Table III are summarized the x-ray findings in this group of nine penicillin-treated and ten control animals.

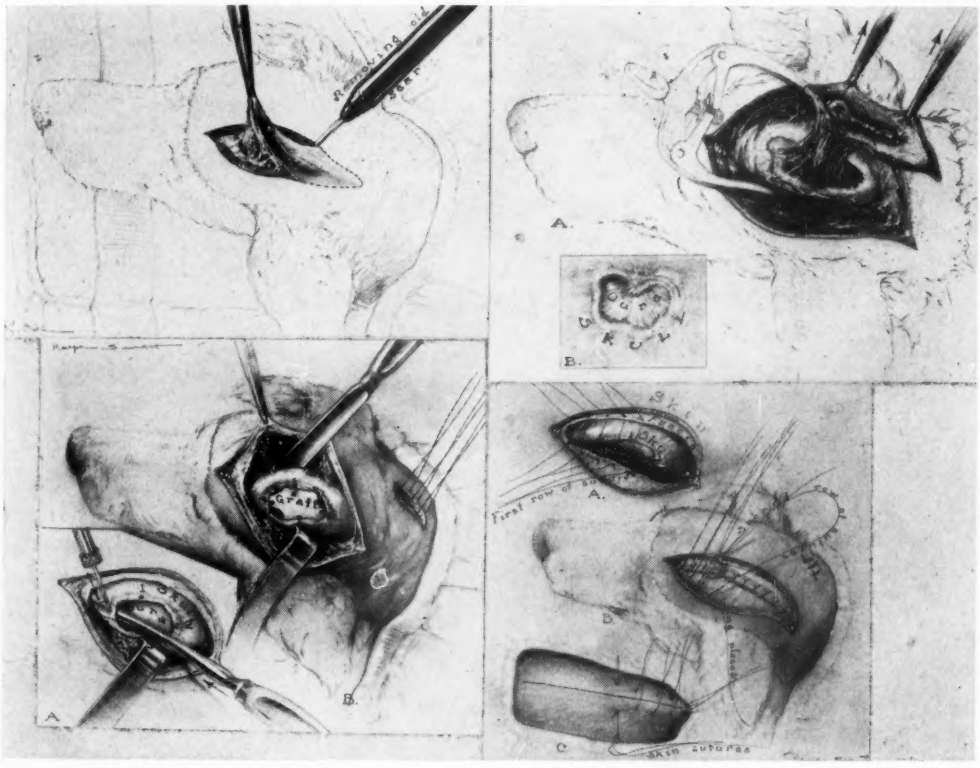

Fig. 2.—Diagrams illustrating method for removal of infected tissues and placing grafts into the skull defects (aseptic surgical technique was used).

The nineteen experimental animals (nine penicillin-treated and ten untreated control animals) were sacrificed six months after the bone grafting operations. In nine penicillin-treated animals full-sized healthy viable bone grafts were found in all cases, although in one graft a very small area beneath a wire had been absorbed, confirming the x-ray findings in the same animal. Bony union between the grafts and the margins of the skull defects was present in eight of the nine penicillin-treated animals. In five of the animals this union was present on all four sides, in one animal union had occurred on three sides,

in two animals on one side, and in one animal there was no bony union, although the graft was viable, of normal size and appearance, and was attached to the skull by fibrous union. In the ten untreated control animals two grafts had been extruded through the infected wound at the time it was open during the early postoperative period, and the skull defects were filled with fibrous tissue in these two animals. In five of the control animals the bone grafts had been extensively absorbed and replaced by scar tissue, although very small residual pieces of bone were imbedded in the scar in two of these animals. One of the control animals had open draining sinuses at the time of necropsy, and the wound contained the black sequestrum of the original graft lying in a bed of infected granulation tissue. The remaining two untreated control animals had healthy viable grafts with bony union on all sides; however, one of these was only a very thin plate of bone. In Table IV are summarized the necropsy findings in nine penicillin-treated and ten untreated control animals six months after the bone grafting operations.

In all animals the gross evidence of bony union between the grafts and the skull defects was confirmed by histologic examination.

In the animals treated with penicillin there was satisfactory healing of soft tissues, survival of the bone grafts, and union between graft and skull, in the presence of both penicillin-susceptible and penicillin-resistant organisms. These results appear significant when contrasted with the suppuration of the soft tissues and absorption or loss of grafts that occurred in most of the untreated control animals.

NEUROFIBROMA OF THE POSTERIOR MEDIASTINUM

I. DARIN PUPPEL, M.D., COLUMBUS, OHIO
(From the Department of Research Surgery of the Ohio State University)

INTRATHORACIC tumors of neurogenic origin are rare, records of 141 cases having been found by me in the literature. There is no doubt that many more exist than have been reported heretofore, as evidenced by the character of the cases collected from various Army Thoracic Surgery Centers in the United States and reported by Blades.[1] Routine roentgenographic examination of the chest led to the detection of more than 85 per cent of the mediastinal tumors in his series. These in many instances presented no clinical manifestations. Of 109 patients who were operated upon for mediastinal tumors over a period of about three years, 29 cases showed benign types of neurogenic origin and each patient was treated successfully by surgical extirpation of the tumor.

Graham and his associates[2] called attention to the real danger of these mediastinal tumors so that now it is generally accepted that benign tumors of neurogenic origin, even though asymptomatic, should be removed to prevent malignant change which so often occurs in the untreated patients. After malignant transformation has appeared, the prognosis often is hopeless and surgical intervention frequently proves curatively ineffective.

At the present time, excision is relatively simple in the usual case of benign tumor and the mortality rate is minimal provided the refined principles of thoracic surgery, of pre- and postoperative care, and of anesthesia are followed. This procedure can be carried out easily even by a general surgeon under proper conditions, provided he applies the principles of modern thoracic surgery.

It has again been emphasized in my patient, as has so often occurred, that roentgenotherapy, which was given elsewhere, proved futile in an attempt to treat the tumor.

CASE REPORT

P. C. (Hosp. No. 453981), a white laborer 61 years of age, was admitted to University Hospital, June 25, 1945. He had minimal symptoms in the chest consisting of mild intermittent dyspnea and an occasional choking sensation particularly when in bed and lying on the right side. Four years prior to admission he was believed to have had heart disease. At that time electrocardiography and roentgenography of the chest were made elsewhere. These revealed what the cardiologist believed to be evidences of coronary heart disease as well as an intrathoracic tumor. The patient was then told that surgical intervention would be dangerous and radiation therapy alone could be considered in treatment of the tumor. Consequently, from July 17 to Aug. 2, 1941, the patient was given over the tumor anteriorly and posteriorly a total of 4,290 roentgen units in sixteen divided daily doses following the technique of Coutard. The tumor proved to be radioresistant and therapy was abandoned. The patient visited several physicians in the next four years who treated him expectantly and without improvement. He became generally nervous, suffered insomnia, and lost about twenty pounds in body weight, principally due to worry about the tumor and his future.

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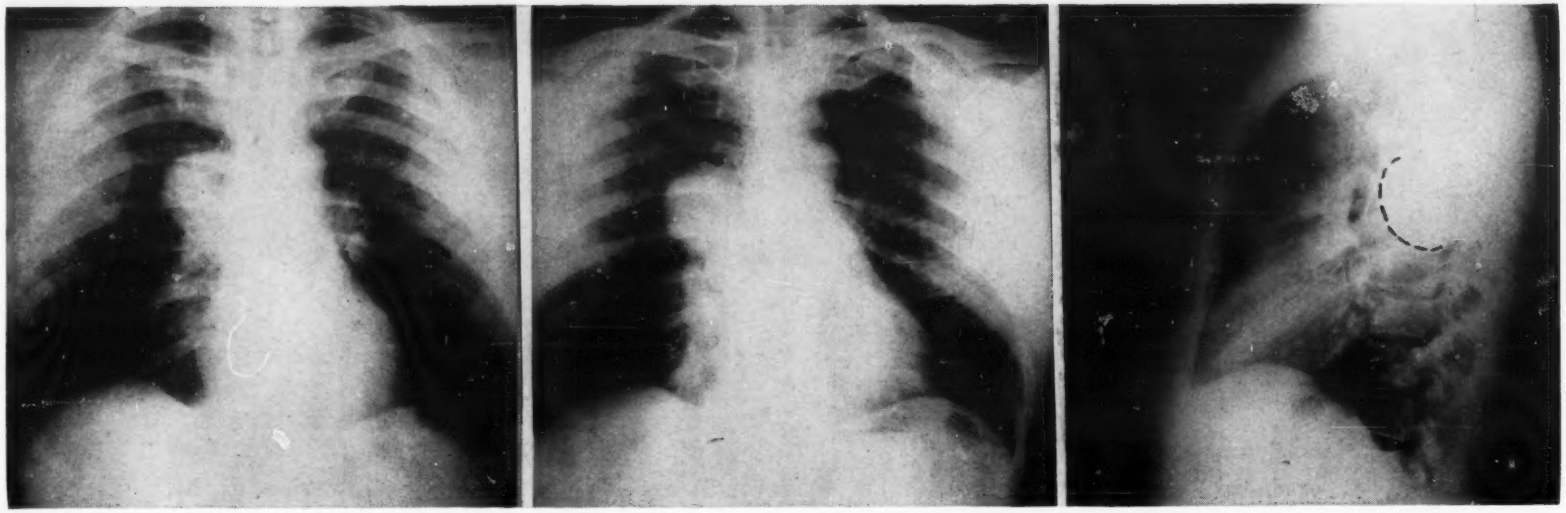

A. *B.* *C.*

Fig. 1.—Anteroposterior and lateral x-ray views of the thorax show the typical position and shape of a primary benign tumor of the posterior mediastinum (*B* and *C*) in 1945 and practically no change in its size when compared to a roentgenogram (*A*) taken in 1941.

I saw him first in June, 1945, at which time a roentgenogram (Fig. 1, *B*) revealed no appreciable change in the size or shape of the tumor when compared to the roentgenogram (Fig. 1, *A*) which was obtained in 1941, prior to the course of x-ray therapy. I advised that he be hospitalized. The rest of the history was not remarkable.

Physical examination disclosed a well-nourished and well-developed white man who was in apparent good health. The thorax was symmetrical and its expansions equal. The lungs were clear to percussion and auscultation. Breath sounds were normal throughout and there were no râles. The heart was not enlarged, its sounds were of good quality, and there were no murmurs present. The remainder of the examination was also negative.

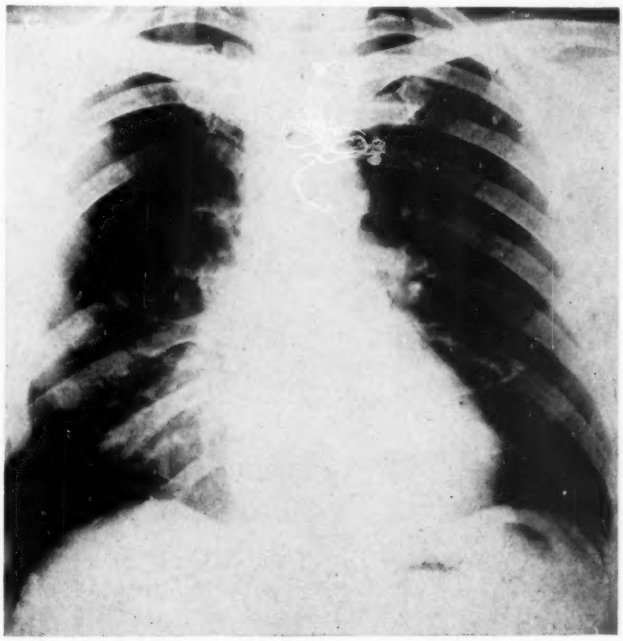

Fig. 2.—This radiogram at six months following operation reveals no abnormalities except for missing segments of the sixth, seventh, and eighth ribs.

On admission the red blood count was 4,310,000, with the hemoglobin 13.2 Gm. per cent. The white blood count was 5,200, with the neutrophiles 63 per cent, lymphocytes 21 per cent, monocytes 7 per cent, and eosinophiles 9 per cent. The urinalysis was negative. The blood Mazzini and Kahn reactions for syphilis were negative. The blood urea nitrogen was 15.5 mg. per cent, which is normal. Phenosulfonphthalein intravenously showed 40 per cent excretion during the first hour and 20 per cent during the second hour, which are normal. An electrocardiogram revealed left axis deviation, slurring of the QRS complexes, deep Q_4 waves, prolonged ventricular conduction, abnormal S-T intervals, and abnormal T waves, which are indicative of myocardial damage with a ventricular conduction defect. Skiagrams of the chest (Fig. 1) showed a sharply circumscribed spherical mass located far posteriorly in the right mediastinum. It extended from the level of the sixth to the ninth ribs posteriorly. It extended anteriorly to just back of the bifurcation of the trachea (Fig. 1, *C*). Radiographs of the spine and ribs were taken, but revealed no gross changes. There were no cord symptoms to suggest a dumbbell type of tumor.

A diagnosis of probable primary benign tumor of neurogenic origin was made and the patient was advised that excision be performed in order to preclude and prevent malignant degeneration. One gram of sulfadiazine and 0.6 Gm. of sodium bicarbonate were administered four times daily beginning June 25. Penicillin was given intramuscularly in doses

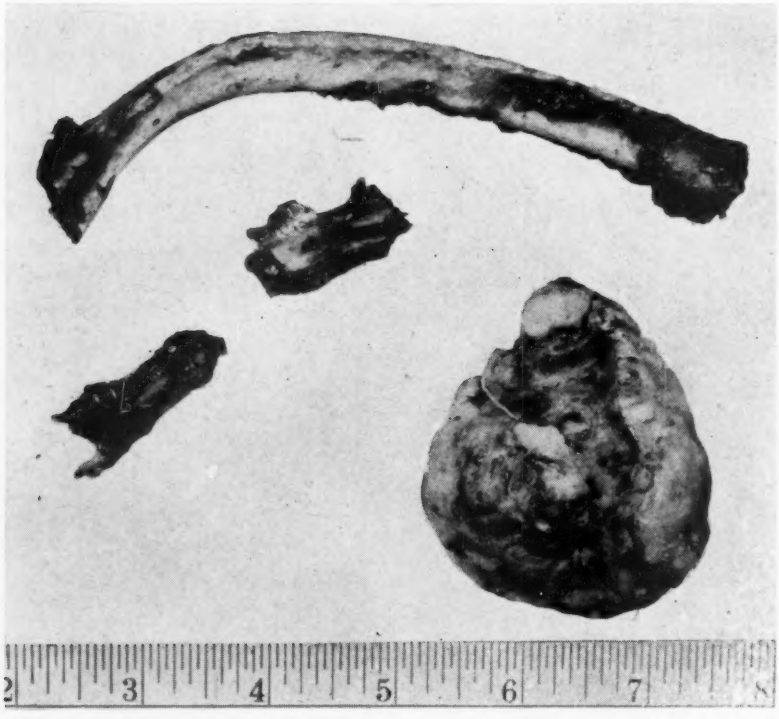

Fig. 3.—The tumor as removed weighed 60 Gm.; it was spherical and well encapsulated. The portions of ribs removed are shown.

Fig. 4.—Cross section revealed a variegated appearance showing areas of old hemorrhage, cyst formation, and yellow tissue in a background of firm grayish tissue.

of 12,500 units every three hours beginning June 27. Adequate amounts of vitamins C and K were furnished.

Under pentothal sodium intravenously for induction and endotracheal anesthesia using cyclopropane, ether, oxygen, and helium, I performed the operation on June 28, using the usual posterolateral approach through the bed of the seventh rib. From the transverse processes outward, 13 cm. of the seventh rib and 2 cm. of each of the sixth and eighth ribs were removed. A retropleural tumor was easily felt in the costovertebral gutter. The pleural cavity was then entered and adequate exposure was obtained by aid of a rib spreader. The tumor was separated from the parietal pleurae by blunt digital dissection. It was tense, spherical, and completely encapsulated. Its pedicle was then visualized and excision was completed by use of multiple clamps, sharp dissection, and adequate hemostasis. During

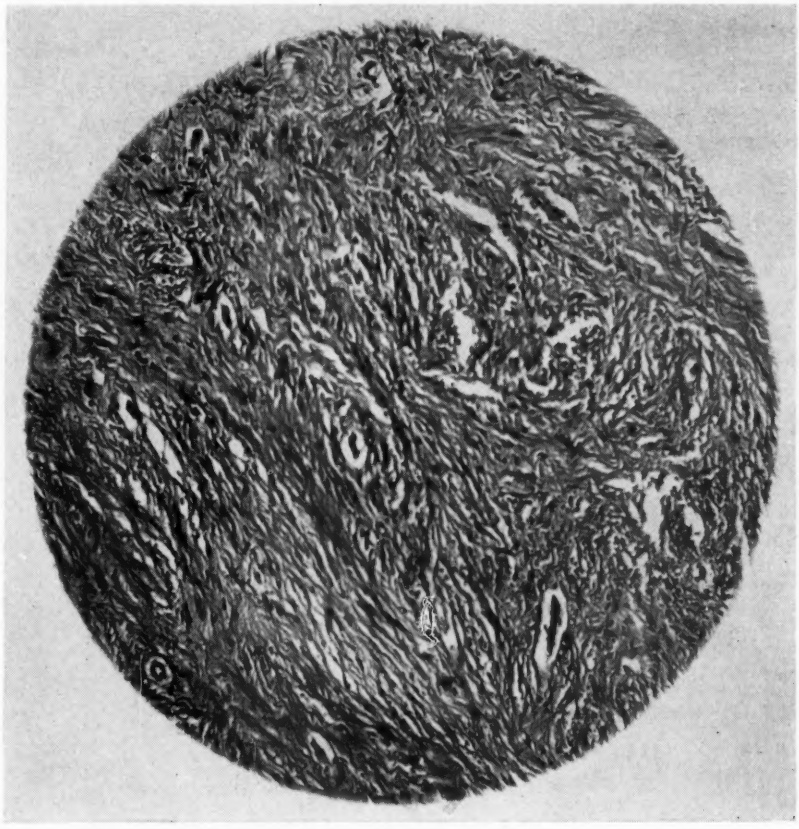

Fig. 5.—Photomicrograph of neurofibromatous tissue.

removal the sympathetic chain and the seventh and eighth intercostal nerves appeared closely associated with the mass. Five grams of sulfathiazole powder and 50,000 units of penicillin were applied in the thoracic cavity. The chest wall was closed in layers without drainage, using interrupted sutures of fine black silk during gradual re-expansion of the right lung. The immediate postoperative condition was excellent. A transfusion of 500 c.c. of whole blood was given during operation. Recovery was uneventful. The patient began to walk on the third day and left the University Hospital on July 5, the seventh postoperative day. He has remained entirely well to date. There have been no dyspnea or choking spells. Nervousness has disappeared. He has regained normal weight. Radiograms at six months (Fig. 2) and at twelve months following operation revealed no abnormalities except for the excised segments of the sixth, seventh, and eighth ribs.

The tumor (Fig. 3) as removed weighed 60 Gm. It was spherical, smooth, well encapsulated, and measured 6 cm. in diameter. The cut surface (Fig. 4) had a variegated appearance showing areas of old hemorrhage, cyst formation, and yellow tissue in a background of firm grayish tissue. Microscopic examination revealed wide variation in the appearance of various serial sections. Hemorrhage and xanthomatous degeneration as well as degenerative changes presumably due to the x-ray therapy were prominent. However, quantitatively the most representative tissue is reproduced in Fig. 5, which is a neurofibroma as shown by special silver staining.

SUMMARY

Roentgenotherapy elsewhere proved futile in the treatment of this mediastinal neurogenic tumor. However, surgical extirpation four years later was relatively easy and proved curative.

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CURARE AND SHOCK: THE PRODUCTION OF HEMORRHAGE INTO THE UPPER INTESTINE OF THE DOG WITH LARGE DOSES OF CURARE

FRANK COLE, M.D.,* DULUTH, MINN., IVAN D. BARONOFSKY, M.D.,† AND OWEN H. WANGENSTEEN, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

CURARE and its alkaloids now are being employed to produce and improve skeletal muscular relaxation during anesthesia for various abdominal operative procedures. In this laboratory recent investigations by one of us (F. C.) of the effects of very large doses of curare in dogs revealed an interesting finding: intense submucosal and mucosal congestion of the entire small and large intestine, with free bleeding into the intestinal tract.[1] The stomachs of these animals did not appear to be congested. Recently, it has been shown that histamine-provoked ulcer or erosion may be accelerated greatly in the experimental animal by venous congestion.[2] The objects of this study were the determination of the mechanism of the development of the intestinal congestion and bleeding, a more detailed examination of the pathologic changes produced by large doses of curare, and an exact knowledge of the effect of large amounts of curare on blood pressure in the experimental animal.

These experiments were performed on eighteen dogs. Intocostrin, a preparation of curare,‡ was used throughout. All injections were intravenous; the entire amount always was given at once, and rapidly. Doses ranged from 0.035 to 1.333 c.c. of Intocostrin per pound of body weight.

Experiment 1.—One Pavlov and two Heidenhain pouch dogs were used. They had been fasted previously for seventeen hours. After fasting, samples were collected, the drug was injected, and specimens were taken. Body weights ranged from 25 to 53 pounds; Intocostrin doses varied from 1.0 to 2.0 c.c. Drooping of the head due to cervical muscle relaxation was encountered in all cases, the animals being suspended in slings. Intercostal muscle paralysis commonly was seen. Cyanosis was present in two cases. A total of three readings was made on the Heidenhain pouch dogs and two on the Pavlov dog. While doing a fourth reading on one of the Heidenhain pouch dogs, the animal died from respiratory paralysis. It was found that there was no stimulation of volume or of free hydrochloric acid in the gastric secretions in the Heidenhain or Pavlov pouch dogs.

Experiment 2.—In two dogs, 10 c.c. of Intocostrin were poured into the jejunum (opened along the antimesenteric border) under intravenous pento-

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*Department of Anesthesiology, St. Mary's Hospital.

†National Cancer Trainee.

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barbital sodium (15 mg. per pound) anesthesia. The Intocostrin was kept there for one-half hour. No bleeding or congestion was noted.

Experiment 3.—Three dogs, whose weights ranged from 22.5 to 43 pounds, were given Intocostrin, in doses from 0.718 to 1.240 c.c. per pound. Tracheal intubation was performed immediately, and artificial respiration was instituted promptly and maintained continuously until the animal died. Entry of the gastric secretions into the duodenum was prevented by putting a strong ligature around the pylorus as soon as possible after curarization (four to ten minutes). In one case a ligature was placed below the entrance of the major pancreatic duct to prevent bile and pancreatic secretions from continuing to enter the small intestine. These dogs died in two to five hours, larger doses of curare being associated with shorter survival times. In all three animals bleeding was found in the small bowel; the hemorrhage was characterized by a gradient, being most marked in the duodenum and least in the ileum. No blood was found in the large intestine. Where ties had been placed between the stomach and duodenum and below the ampulla of Vater, the closed duodenal loop was found to be intensely hemorrhagic, as was the entire jejunum and ileum. In this animal the appendix was markedly hemorrhagic.

Experiment 4.—Minimal lethal doses of curare (0.065 and 0.067 c.c. of Intocostrin per pound of body weight) were administered to two dogs. Artificial respiration was not performed. Post-mortem examination of these animals revealed (1) normal intestines and (2) apparently an increased amount of intestinal secretions, particularly in the small bowel.

Experiment 5.—Pentobarbital sodium solution (15 mg. per pound) was injected intravenously in two dogs. The trachea was promptly intubated, using a wide-bore rubber tube with an inflatable cuff, and continuous artificial respiration was instituted immediately. A cannula was then inserted into the right common carotid artery and kymographic blood pressure recordings were made. Massive doses of Intocostrin (1.3 and 1.4 c.c. per pound) were injected. Immediately following (within five seconds) the injection of curare, the arterial blood pressure fell from 165 and from 130 mm. Hg, systolic to 10 to 12 mm. Hg. The blood pressure fall then continued at a slower rate until no pulse or pressure existed; death occurred in twenty-two minutes in one case and sixty-eight minutes in the other (Fig. 1). Gross autopsy findings included the following: (1) normal stomach, (2) bleeding and congestion in the small intestine, most marked in the duodenum and upper jejunum and least in the ileum, (3) apparently normal large bowel, (4) congestion of the pancreas and spleen, and (5) bilateral pulmonary atelectasis and congestion.

Experiment 6.—Using two dogs, the technique carried out in Experiment 5 was repeated. When the fall in blood pressure occurred following the administration of curare, ephedrine and epinephrine solutions were administered intravenously (and intramuscularly before curarization) in amounts sufficient to eliminate shock. It was found that very large amounts of vasoconstricting drugs were required to prevent the occurrence of shock. In one dog, 110 mg. of ephedrine and 4 mg. of epinephrine were administered within two hours.

It was noted that (1) the blood pressure could always be raised by the administration of a vasoconstricting agent, (2) the stimulation of blood pressure lasted only one or two minutes at times, and (3) epinephrine produced a more effectual blood pressure rise than ephedrine (Fig. 2). The animals were sacrificed in two and in four hours. At autopsy, some pulmonary atelectasis and congestion were seen; the intestines appeared to be normal.

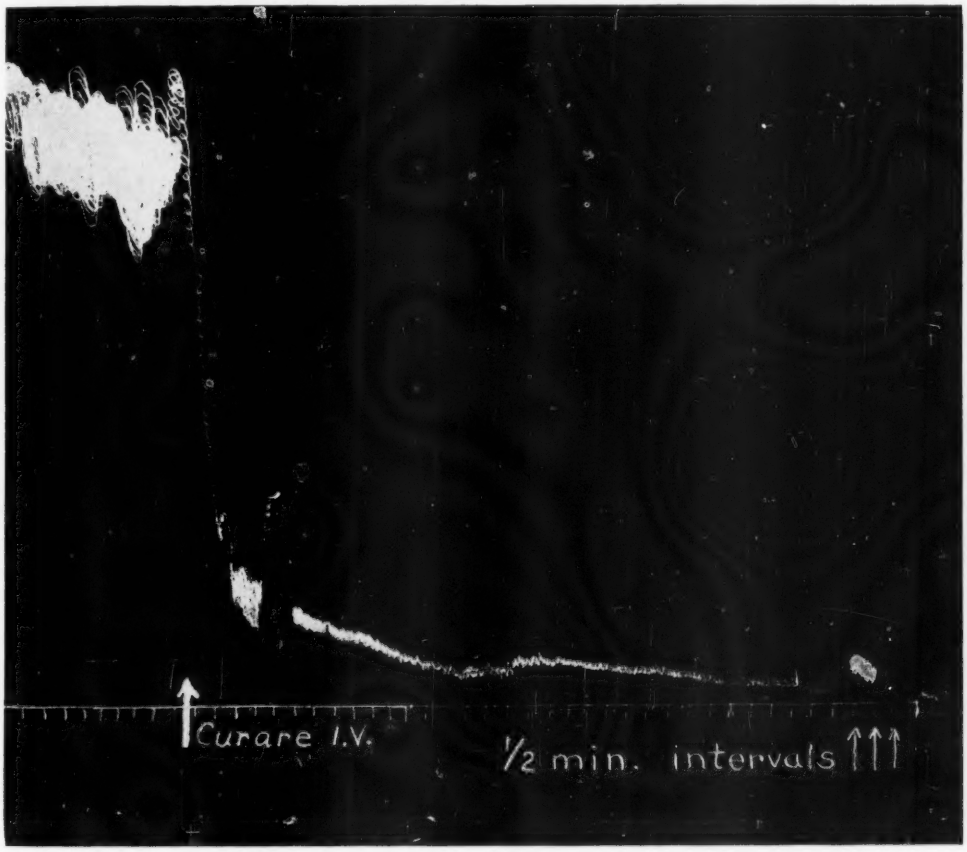

Fig. 1.—Effect of large dose of curare on arterial blood pressure.

Experiment 7.—Two dogs weighing 14 pounds were anesthetized by the intravenous injection of sodium pentobarbital. Each then received 3 c.c. of heparin intravenously. A needle was inserted into a vein and connected to a manometer, then 10.5 c.c. of Intocostin (0.750 c.c. per pound) were administered intravenously in each case, and artificial respiration was performed. No change in venous pressure occurred following curarization. Venous pressures varied between 6 and 8 cm. Post-mortem examination showed congestion of the intestines in both dogs. One animal had atelectasis of one lobe, the other had a patchy atelectasis of both lungs.

Experiment 8.—A dog weighing 20 pounds received 400 mg. of sodium pentobarbital intravenously. The trachea was intubated and an artery was

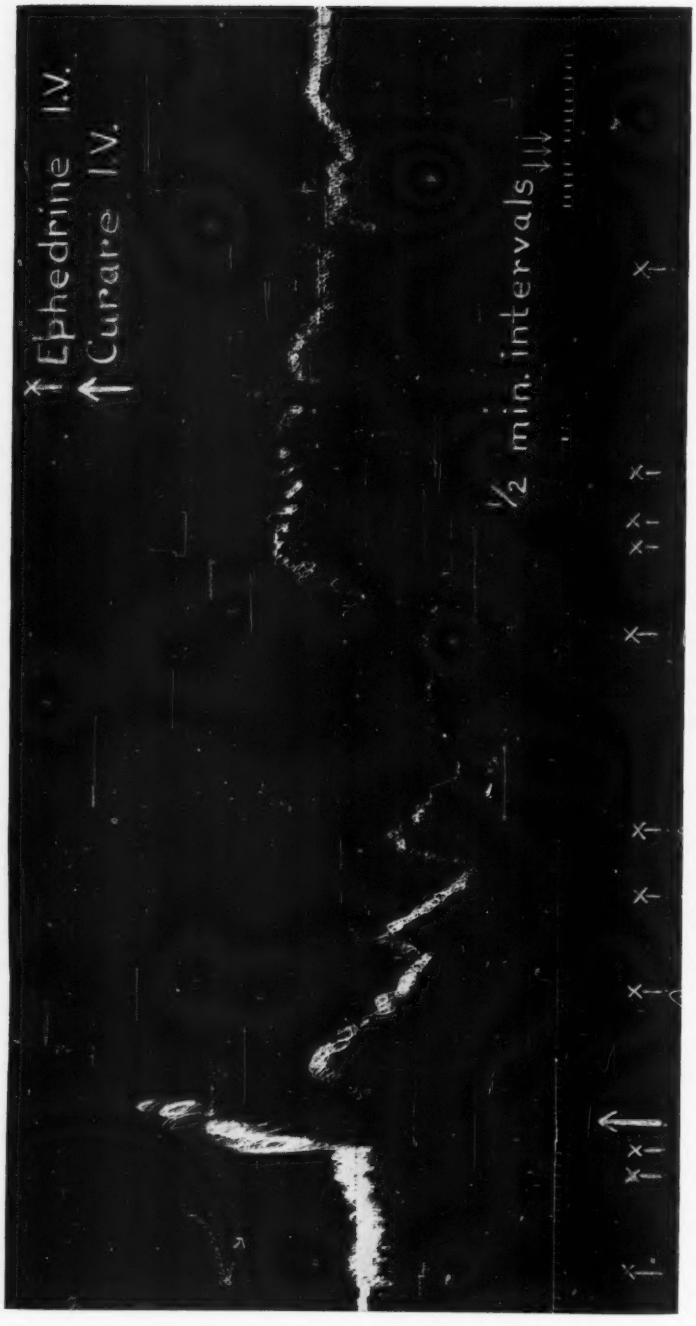

Fig. 2.—Record of arterial blood pressure after administration of massive dose of curare, where vasoconstricting drugs were administered.

cannulated. A blood transfusion was started very slowly. Three cubic centimeters of heparin were injected intravenously to prevent clotting in the venous pressure tube, eliminating the need for citrate solution. A venous pressure apparatus was set up; the reading at this time was 1.2 cm. Just after the flow of blood was increased, 15 c.c. of Intocostrin were injected intravenously so that it passed through the drip bulb in a steady stream. The arterial blood pressure fell rapidly to 10 mm. Hg, then gradually to zero. At this time, while artificial respiration was being performed, the venous pressure rose slightly, to 2.5 cm. Three hundred cubic centimeters of whole blood were injected.

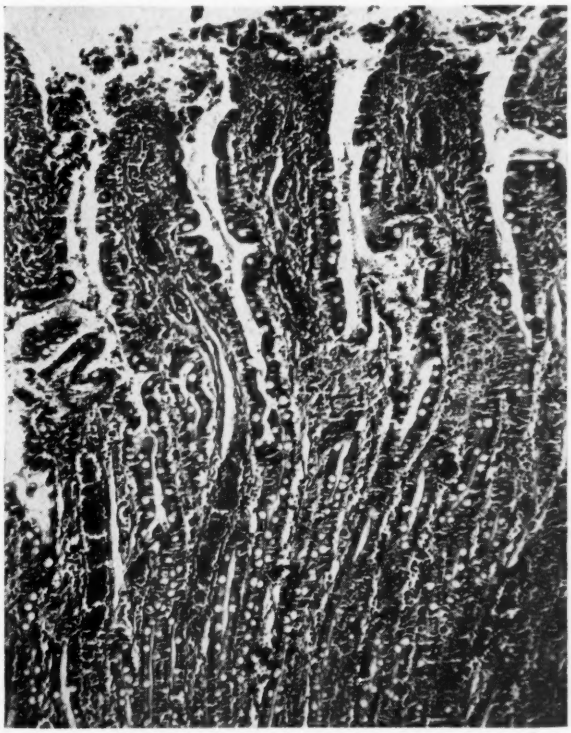

Fig. 3.—Small intestines of dogs receiving 1.0 c.c. of Intocostrin per pound and continuous artificial respiration. Note hemorrhage and engorgement of vessels (×80).

The same technique was carried out in a dog weighing 16 pounds. This animal was given 12 c.c. of Intocostrin (0.750 c.c. per pound). It was found immediately following curarization that there was considerable difficulty in inflating the lungs. The arterial blood pressure fell immediately on curarization; the venous pressure rose gradually and steadily to 18 cm. During this time about 325 c.c. of whole blood were injected rapidly in ten to fifteen minutes.

Microscopic studies of sections of various splanchnic viscera (stomach, intestines, pancreas, spleen, liver, lungs, adrenals, and kidneys) in the dogs receiving lethal doses of curare and artificial respiration in Experiments 3, 5, and 6 revealed interesting findings. Those animals given intravenous curare and artificial respiration, with no attempt being made at raising the blood pressure (Experiments 3 and 5), showed intense engorgement of the intestinal

capillaries and venules of the mucosa and submucosa (Fig. 3). The only organs studied that were not affected were the adrenals and stomach. In those animals receiving a vasoconstricting drug in addition (Experiment 6), no gross or microscopic evidence of hemorrhage or congestion was seen (Fig. 4). The lungs, however, appeared congested. These findings were in contrast to those in the animals in which the blood pressure was allowed to fall. The dogs receiving apneic doses of curare showed no congestion.

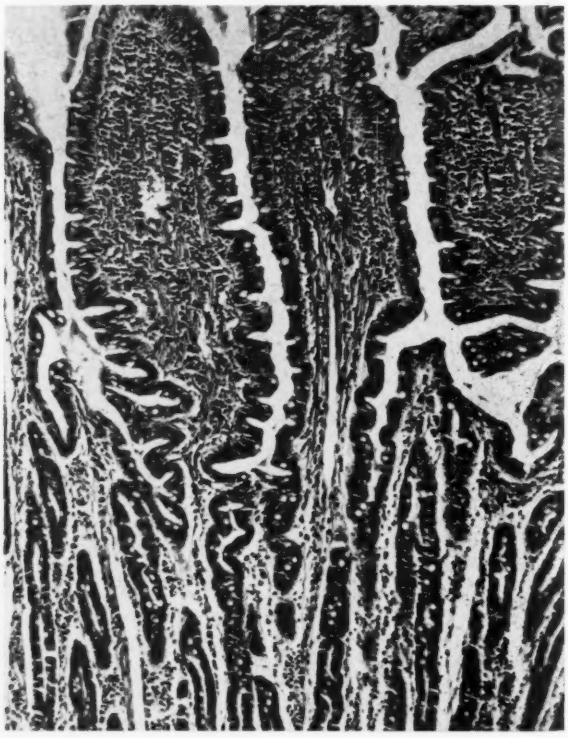

Fig. 4.—Intestines of dogs receiving massive doses of curare where vasoconstricting drugs were administered (×80).

COMMENT

The lack of stimulation of gastric secretions by somewhat larger than therapeutic doses of curare (0.035 to 0.040 c.c. of Intocostrin per pound) and the consistent finding of mucosal intestinal hemorrhage and congestion after exclusion of gastric juice as well as after the simultaneous exclusion of gastric, biliary, and pancreatic digestive juices from the jejunum suggest that the intestinal bleeding and congestion caused by such doses of curare are not brought about by the digestive secretions. That the intestinal congestion is not due to a local effect of curare was demonstrated in Experiment 2. It was shown in Experiment 4 that very large amounts of curare were required to produce the pathologic changes described; smaller (minimal lethal) doses produced no such changes. It must be noted, however, that the deaths following

these smaller doses occurred within thirteen and thirty minutes following curarization.

Experiments 5 and 6 show that (1) injections of very large amounts of curare can produce a rapid and fatal fall in blood pressure, (2) the hypotension can be corrected by the administration of vasoconstricting drugs, and (3) intestinal bleeding occurs (when large amounts of curare have been injected) when shock is produced and does not occur when the systolic blood pressure is maintained at a level of 80 to 90 mm. Hg. The failure of the venous pressure to rise (Experiment 7) and the failure of the blood pressure to increase after rapid blood transfusion (Experiment 8) can be explained by the pharmacologic actions of curare. This drug depresses the vasomotor center and ganglia.[3] Thus, the potential "lake" formed by the dilatation of these organs cannot be filled fast enough, and little, if any, blood returns to the heart. The heart itself is affected by large doses of curare,[4] and this occurrence in itself thus will prevent a blood pressure rise after transfusion. The intestinal pathology found after the administration of very large amounts of curare thus would seem to be consequent on the production of shock and on this basis alone. Freeman and associates[5] have shown that in the shocked dog the superficial portion of the mucous membrane of the intestine can disappear. In fact, during periods of low blood pressure the dogs always had profuse diarrhea in which sloughs of mucous membrane could be made out. It has been shown[6, 7] that in the dog congestion of the liver, spleen, kidneys, and intestinal mucosa are present following death caused by shock. That sometimes a considerable amount of time is required for the formation of the pathologic changes described has been demonstrated by this study and by others. Dunphy and co-workers[8] have shown in their study of experimental traumatic shock that intestinal hyperemia, submucosal hemorrhage, and duodenal or jejunal ulcerations were found in late shock (six to twelve hours) and were not present in early shock.

These results suggest the necessity for close scrutiny of the doses used in man. It has been shown[1] that the minimal lethal dose of Intocostrin in the dog is 0.065 c.c. per pound of body weight. If artificial respiration is performed, pathologic changes appear with doses of 0.650 c.c. per pound (possibly earlier). Dogs can be killed by doses of 1.3 c.c. per pound, even when artificial respiration is maintained. In man, 0.025 c.c. of Intocostrin per pound[3] is commonly injected; as much as 0.20 c.c. per pound has been administered, although not at once. Doses sufficient to produce muscular relaxation and respiratory depression appear to be nearly alike, in proportion to body weight, in man and in the dog; the dog, however, seems able to withstand anoxia better.

CONCLUSIONS

1. Large doses of curare (0.718 to 1.240 c.c. per pound), when administered intravenously in single injections to dogs kept alive by artificial respiration for two to five hours, produce congestion and hemorrhage in the intestinal mucosa.

2. Curare does not stimulate gastric secretion.

3. Exclusion of the gastric juice from the intestine does not prevent the mucosal intestinal hemorrhage.

4. The topical application of curare to the mucosa of the small intestine does not produce gross congestion.

5. Dogs receiving large doses of curare exhibit severe depression of arterial blood pressure but no appreciable change in venous blood pressure.

6. Vasoconstricting drugs obviate the fall in blood pressure attending the intravenous injection of large amounts of curare; rapid transfusions of whole blood lack this effect.

7. When shock is averted, intestinal hemorrhage is not seen. Shock is therefore the most likely cause of the intestinal hemorrhage attending the intravenous injection of large amounts of curare.

The authors take this means of thanking Dr. Maurice Visscher and Dr. W. G. Kubicek, of the Department of Physiology, for their valuable comments; Professor E. T. Bell, of the Pathology Department, for kindly reviewing the sections of organs removed for post-mortem examination; and Dr. Harold Baronofsky, of the School of Dentistry, for his technical assistance.

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POSTOPERATIVE PROTEIN DEFICIENCY

With Special Reference to the Cancer Patient

H. M. Wiley, M.D.,* Columbia, Mo.

(From the Department of Surgery, Ellis Fischel State Cancer Hospital)

A GREAT deal of investigation has been carried out during the last few years on serum protein. Due to this work it has become increasingly evident that low serum protein can, and does, lead to many clinical complications, some of serious nature. The resulting ill effect of hypoproteinemia in the postoperative case has increasingly put the surgeon on guard. Among these complications the following may be noted:

1. The healing of wounds is retarded in the presence of low serum protein. The growth rate of fibroblasts in wounds is increased by high protein diets.[1]

2. Actual wound disruption may, at times, be due to hypoproteinemia.[2]

3. The relationship of edema to this condition is well established. The surgeon should remember that clinical edema, usually, does not appear until approximately a 10 per cent increase in body weight has occurred.[3]

4. A decreased gastrointestinal motility may result from a hypoproteinemic state, and actual obstruction may occur about an intestinal anastomosis, because of local edema resulting from a low blood protein.[4]

5. Increased susceptibility to the toxic effects of anesthesia may be due to low serum protein.[5]

6. Susceptibility to infection is, also, increased by this biologic imbalance and, as has been shown by Whipple[6] and others, infection may check completely the plasma protein production.

From these, the surgical importance of hypoproteinemia becomes apparent. The studies presented here show the high incidence of postoperative hypoproteinemia, especially as it occurs in cancer patients.

Method and Result of Study.—A total of fifty-seven patients who underwent surgical procedures were studied. Forty-five of these operations were for cancer and twelve were for benign conditions, but all were major procedures. The average age in this group of patients was 57.6 years. Preoperative serum protein determinations were obtained and, at least, three total and fractional measurements were made within the first ten postoperative days. Twenty-one of the cancer patients had determinations made of the liver functions, as measured by the Quick hippuric acid liver function test.[7] Throughout the study, hydration of these patients was carefully maintained by accurate intake and output records, plus hematocrit determinations in most cases. Caution should be observed in interpreting serum protein values, because of the possible influence of dehydration. Not infrequently, patients have been seen with ap-

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*Trainee, National Cancer Institute, and Resident in Surgery.

TABLE I. NUMBER AND TYPES OF OPERATIONS WITH THE PREOPERATIVE TOTAL PROTEIN AND THE MAXIMUM DECLINE OR RISE IN SERUM PROTEIN IN THE FIRST TEN DAYS POSTOPERATIVE*

OPERATION	PREOPERATIVE SERUM PROTEIN	MAXIMUM NUMBER OF GRAMS LOSS OR GAIN IN SERUM PROTEIN POSTOPERATIVE	
		MALIGNANT CONDITIONS	BENIGN CONDITIONS
Large bowel procedure, abdominoperineal rectal resection [one-stage (10)]	6.2	- 1.5	
	6.1	- 1.6	
	7.1	- 2.6	
	7.7	- 2.4	
	6.3	- 1.7	
	6.4	- 1.5	
	6.5	- 2.3	
	6.4	- 0.4	
	6.0	- 1.6	
	6.2	- 1.2	
Two-stage abdominoperineal rectal resections (1)			
First stage	7.0	- 1.2	
Second stage	8.0	- 2.8	
Right colectomy (1)	5.7	+ 0.8	
Sigmoid colon resection (1)	6.7	- 2.0	
Cecostomy (1)	7.7	- 2.1	
Transverse colon resection (1)	7.4	- 2.9	
Radical mastectomies (12)	6.4	- 0.6	
	8.1	- 2.4	
	6.6	- 2.6	
	7.4	- 2.7	
	6.3	- 2.0	
	6.6	- 2.2	
	5.8	- 1.7	
	6.3	- 0.8	
	7.8	- 1.7	
	6.8	- 0.9	
	6.7	- 0.4	
	7.3	- 1.6	
Subtotal gastric resections (6)	6.1	- 0.7	
	7.9	- 3.2	
	4.7	+ 3.7	
	6.7		- 1.8
	5.0		- 1.2
	5.9		+ 1.2
Exploratory laparotomy (3)	4.9	- 0.1	
	5.4	- 1.0	
	5.6		- 0.9
Radical neck dissection (5)	7.6	- 0.2	
	7.0	- 2.0	
	5.8	+ 1.2	
	6.8	- 0.7	
	6.3	- 1.3	
Jaw resection (2)	6.9	- 2.1	
	6.1	- 1.5	
Gynecologic procedures (5)	7.4	- 2.1	
	6.6	- 1.8	
	6.2		- 1.6
	6.1		- 0.8
	7.3		- 1.8

*Minus or plus sign indicates fall or rise, respectively, in serum protein from the preoperative level.

TABLE I—CONT'D

OPERATION	PREOPERATIVE SERUM PROTEIN	MAXIMUM NUMBER OF GRAMS LOSS OR GAIN IN SERUM PROTEIN POSTOPERATIVE	
		MALIGNANT CONDITIONS	BENIGN CONDITIONS
Subtotal thyroidectomy (2)	6.1		- 1.6
	6.8		- 1.5
Biliary tract (1)	7.5		- 2.5
Nephrectomy (1)	6.3	- 0.8	
Axillary dissection (1)	7.3	- 0.3	
Excision of esophageal diverticulum (1)	7.1		- 1.3
Hemipelvectomy (1)	6.3		+ 2.2
Bilateral groin dissection (1)	6.1	- 1.4	
Total		45	12

parently normal, or even elevated, total protein values which show a marked fall following proper hydration. A loss of 6 per cent or more of body weight is necessary before clinical dehydration is apparent.[8] In Table I are listed the number and different types of operations that were studied; the maximum drop or gain in total proteins during the first ten days after operation is shown.

Of the forty-five patients with cancer, twenty (44 per cent) had total protein values below 6.5 Gm. per cent on admission. Robillard and Shapiro[9] found 55 per cent of their cancer patients, upon whom surgery was contemplated, to have values below 6.5 Gm. per cent. In studies on gastric carcinoma, Abel and co-workers[10] found 59 per cent with abnormally low serum protein levels. Of six gastric carcinomas explored or resected in this group, four had total protein values below 6.5 Gm. per cent.

Of the forty-five patients operated on for malignancy, forty-two (93 per cent) showed a postoperative drop in serum proteins. In twelve patients not having cancer, ten (83 per cent) showed a fall in serum proteins. Casten and co-workers[5] have noted the following incidence of decline in plasma protein in benign conditions: Appendectomy for acute appendicitis showed a decrease in 69.6 per cent of the cases, and cholecystectomy, for cholecystitis or cholelithiasis, 81.6 per cent.

Of the forty-two cancer patients showing a postoperative fall in total proteins, the decrease was due to a drop in the albumin fraction in sixteen cases, to globulin decline in seven cases, and to a fall in both albumin and globulin in nineteen cases (Table II).

TABLE II. DECLINE OF TOTAL PROTEIN DUE TO ALBUMIN, GLOBULIN, OR ALBUMIN AND GLOBULIN

SERUM PROTEIN FALL DUE TO	NUMBER OF PATIENTS (42)	PER CENT
A. Albumin	16	38
B. Globulin	7	16.7
C. Albumin and globulin	19	45.3

Kagan[11] has found that a decrease in total protein concentration below normal is due, almost invariably, to a decrease in the albumin fraction. Elman and Lischer[12] have also emphasized this. The observations made here do not entirely verify their conclusions, as the globulin fraction, also, fluctuates, especially if there is an associated infection. Of sixteen patients who had foci of infection in either the chest, or wound, or a phlebitis, twelve showed a rise in the globulin fraction postoperatively. Kagan[13] has stressed the relationship of hyperglobulinemia to infection.

The fact that twenty-six or approximately 61 per cent (sum of B and C, Table II), of these patients showing a serum protein fall had a decrease in the globulin fraction emphasized the clinical significance of the work of Cannon and associates.[14] They have directed attention to the role of globulin (especially the gamma fraction) depletion to reduced resistance to infection, and the origin of globulin from dietary amino acids.

The greatest postoperative rise in serum protein was 3.7 Gm. per cent. This rise was due to a marked increase in globulin, from 1.9 Gm. preoperatively to 5.7 Gm. per cent on the ninth postoperative day. Roentgenograms of this patient's chest at the time showed an extensive bronchopneumonia.

The greatest decline in serum protein in this study was 3.2 Gm. per cent, occurring in a patient after a gastric resection for carcinoma. This patient's preoperative serum protein studies showed a total of 7.9 Gm. per cent, with a fractional breakdown of albumin 3.8 Gm. per cent, and the globulin 4.1 Gm. per cent. The greatest recorded drop occurred on the fifth day after operation with a total of 4.7 Gm. per cent, made up of 3.4 Gm. per cent albumin, and 1.3 Gm. per cent of globulin. It will be noted that the decrease is primarily due to a fall in the globulin fraction. This patient's postoperative course was uneventful, with the greatest temperature elevation being 100.4° F. on one occasion. These findings emphasize the need of obtaining fractional serum protein determinations.

Only fifteen (35 per cent) of the forty-two cancer patients who showed a decline in serum protein postoperatively had recovered their initial total protein by the tenth day after surgery.

Of the cancer patients showing a postoperative decline in total protein, the average fall was 1.33 Gm. per cent by the third day, 1.32 Gm. per cent by the fifth day, and 1.17 Gm. per cent by the tenth day; and of the benign conditions showing a postoperative fall, the average decline was 0.98 Gm. per cent on the third day, 1.03 Gm. per cent on the fifth day, and 0.76 Gm. per cent on the tenth day after surgery (Fig. 1). This observation shows a slightly greater decline in serum protein concentration in cancer patients than in patients with noncancerous lesions. From this study, it is not possible to say how long it takes for the serum total protein to return to normal levels after operation.

Operations on the gastrointestinal tract, for malignant lesions, showed a decline in serum protein postoperatively in eighteen out of twenty cases. Of the ten one-stage abdominoperineal resections, all but one patient showed a drop of over 1 Gm. in the total serum protein level. Five of these had regained their

preoperative level by the tenth postoperative day. Twelve patients with radical mastectomies showed a total protein decline ranging from 0.4 to 2.7 Gm. per cent after operation. Of this latter group, only two had recovered the preoperative total protein level by the tenth postoperative day.

The small per cent of patients showing recovery within ten days, to the preoperative serum protein level, after radical mastectomy is of interest, as they are usually taking a surgical soft diet on the first day after operation and are frequently on a regular diet by the second day. It follows that these patients are on an insufficient caloric intake for only one or, at most, two days after surgery. Accordingly, it is felt that starvation per se does not entirely account for the postoperative decline in total serum proteins following radical mastectomy.

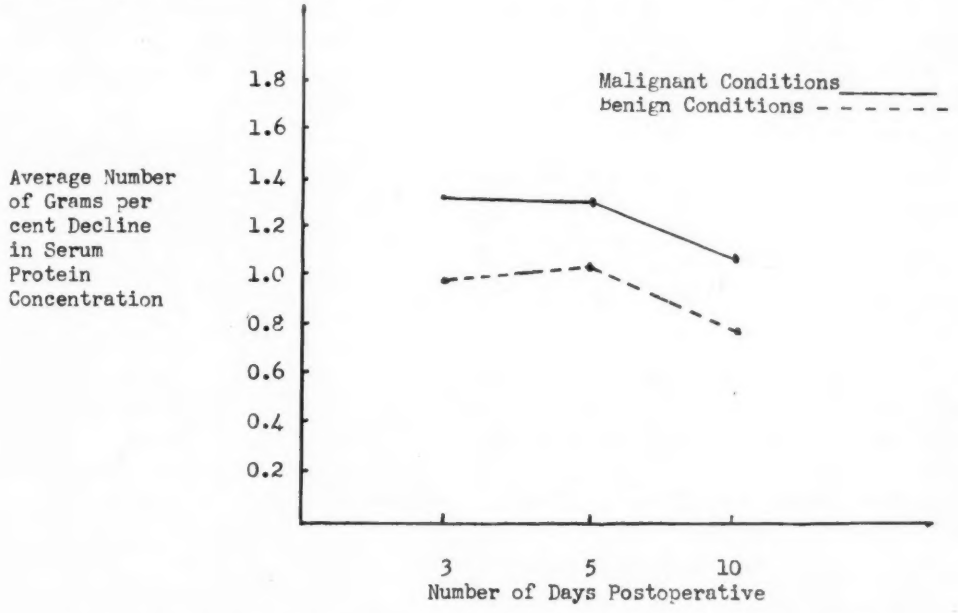

Fig. 1.—Average fall in serum proteins on third, fifth, and tenth postoperative days.

In patients who have undergone a major surgical procedure there is frequently considerable blood loss, which may partially account for the total serum protein fall. Of thirty-one cancer patients, in whom both preoperative and postoperative hemoglobin determinations were available, twenty-seven patients showed a fall both in hemoglobin and in serum protein. Four patients showed a rise in hemoglobin and a fall in the serum protein. All of those who showed a rise in hemoglobin received one or more blood transfusions during, or immediately after, operation. Coller and co-workers[15] reported on the blood loss following various operative procedures. In radical mastectomies they found an average loss of 732 c.c. in twenty operations, compiled from various authors' reports. As stated previously, all radical mastectomies in this study showed a postoperative decline in serum protein concentration. Many of these patients were in an excellent state of nutrition, which might suggest that the serum protein drop was largely due to blood loss per se. However, if the ratio of one

to thirty[12] of serum protein to body protein is remembered, even a loss of several hundred cubic centimeters of blood will not account for the entire fall in serum protein in all cases. Whipple[16] has shown that a "dynamic equilibrium" exists between the body and blood proteins, the body giving up protein to the blood stream when blood is lost, so that the one to thirty ratio is maintained. Thus, if 700 c.c. of blood are lost, and the preoperative serum protein level was 7 Gm. per cent, this would represent a loss of 49 Gm. of protein. It can be calculated that an individual weighing seventy kilograms would have to lose 75 Gm. of protein to reduce the serum protein to 5.5 Gm. per cent. In the twelve radical mastectomies studied here, eight patients showed a loss in serum protein greater than the calculated loss from bleeding at operation alone, the differences being quite marked in several cases (Table III). From these findings it is apparent that the blood loss at operation does not entirely account for the total serum protein loss. The explanation of this loss is not entirely known. However, it is felt[17] that the more important factors are a decreased protein intake and an enhanced protein catabolism. Elman[18] has shown that most fasting patients excrete about 4 to 5 Gm. of nitrogen a day when sufficient glucose is ingested to meet the caloric needs. Postoperatively, he noted a rise in urinary output of nitrogen in some cases to as much as 26 Gm. per day. This would correspond to the catabolism of 162.5 Gm. of protein. The influence of anesthesia may bear some relationship to postoperative serum protein decline and should be investigated.

TABLE III. DIFFERENCE BETWEEN THE CALCULATED PROTEIN LOSS FROM BLEEDING AT OPERATION AND THE ACTUAL PROTEIN LOSS

PATIENT	WEIGHT (IN KG.)	PREOPERATIVE SERUM PROTEIN (GM. PER CENT)	MAXIMUM POSTOPERATIVE SERUM PROTEIN DROP (GM.)	CALCULATED BLOOD VOLUME IN C.C. ($\frac{1}{13}$ OF BODY WEIGHT)	CALCULATED PROTEIN LOSS FROM BLEEDING (GM.)	ACTUAL PROTEIN LOSS (G.M.)	DIFFERENCE BETWEEN BLEEDING LOSS AND ACTUAL LOSS (GM.)*
27	60	6.6	2.2	4,600	46.2	101.2	55.0
53	50.8	7.4	2.7	3,900	51.8	105.3	53.5
35	96.3	6.4	0.6	7,300	44.8	43.8	+1.00
44	77.7	6.6	2.6	5,900	42.2	153.4	111.2
1	58.1	6.7	0.4	4,400	46.9	17.6	+29.3
22	67.2	6.8	0.9	5,100	47.6	45.9	+1.7
33	58	7.8	1.7	4,400	55.6	74.8	19.2
32	68	8.1	2.4	5,300	56.7	127.2	70 5
6	54.5	7.3	1.6	4,190	51.1	67.06	15.96
17	62.7	6.4	1.7	4,820	44.8	81.94	37.14
9	65.9	6.3	0.8	5,070	44.1	40.56	+3.54
29	63.6	6.3	2.0	4,900	44.1	98.0	53.9

*Plus sign indicates bleeding protein loss to be greater than actual loss.

It is felt that in patients with "subnormal" serum protein concentrations that the body protein reserves are, also, bordering on depletion. When such a patient is subject to an acute nutritional emergency, for example, operation, traumatic injury, and anesthesia, and the resulting enhanced protein catabolism, the body protein reserve is quickly exhausted and is reflected in a lowered serum protein concentration. In contrast to this acute nutritional insufficiency, a

chronic caloric deficiency may not be reflected by the serum protein level for some time, because of the relatively slow exhaustion of the body protein reservoir.

Of twenty-two patients who had preoperative and postoperative hippuric acid determinations, no conclusive relationship between changes in liver function, as measured by this test, and variations in the serum protein were apparent. Casten and associates[5] in a large group of patients, found that the presence of subnormal hippuric acid excretion was of value in predicting postoperative protein decline.

It is known that the various amino acids are metabolized in different ways by different tissues, for their own specific needs, producing muscle protein, hormones, etc.; others are deaminized in the liver or kidney.[19] Accordingly, it is felt that of the many liver function tests, each measures only one specific function of that organ, and none of the present known tests specifically measure the ability of the liver to utilize proteins; there are no known tests for measuring the ability of other tissues to utilize protein.

Treatment.—In the treatment of the hypoproteinemic state, two factors must be considered: one, the lowered serum and body protein, and two, the impaired liver function which may be present. From a practical standpoint, it is almost impossible to provide enough protein for the body needs, except when taken by way of the alimentary tract. It is generally stated that 1 Gm. of protein per kilogram of body weight a day is necessary to maintain nitrogen balance. However, this amount will furnish only the daily requirements in a person whose previous nutrition has been adequate. Patients with a decreased protein reserve should receive more than 1 Gm. of protein per kilogram of body weight. Knowing that the ratio of serum protein to body protein is approximately one to thirty, it can be calculated that to raise the total protein from 5 to 7 Gm. per cent, in an individual weighing seventy kilograms, it will require approximately 331 Gm. of protein. If a patient ingested and assimilated 1½ Gm. of protein per day, per kilogram, for ten days, it would theoretically elevate the total serum protein from 5 to 7 Gm. per cent, provided sufficient calories were available from carbohydrates and fats to meet the daily requirement. Patients with a lowered protein reserve will probably, also, have depletion of their glycogen reserve,[12] and will require at least 3,000 calories per day. A diet of 3,000 calories consisting of 70 per cent carbohydrates, 5 per cent fat, and 25 per cent protein will provide an excess of protein and can be readily assimilated. The experience of Cuthbertson[20] is of note, as he was unable to eliminate the period of postoperative negative balance, with diets containing as high as 230 Gm. of protein and 4,100 calories.

All too frequently it is impossible for patients to take an adequate diet by mouth preoperatively and for a varying number of days postoperatively. In these cases one is left with two alternatives, jejunal alimentation or parenteral replacement.

Jejunal alimentation is an old method of feeding, which has recently been re-emphasized by Colp and Druckerman.[21] This method of feeding consists of placing a catheter in the upper jejunum (Witzel procedure). After twenty-

four to forty-eight hours patients can be fed a liquid diet through this tube. It may be done as a preliminary procedure to prepare patients for subsequent surgery or as a complementary procedure at the time of surgery. Experience here has not found it possible to prevent postoperative serum protein decline by jejunal feeding, nor, when used as a preliminary procedure, to raise appreciably the serum protein concentration.

A number of good formulas are available for tube feeding. Colp and Druckerman[21] used the Scott-Ivy formula. A recent product,* prepared by a commercial house, would be excellent for this purpose. It yields 4.7 calories per gram. It was originally prepared as a food for undernourished infants and is marketed as such.

The formula used for the experiments described in this paper is shown in Table IV. This formula has proved quite satisfactory without causing diarrhea, distention, or other notable ill effects. It contains approximately 1.5 calories per cubic centimeter. Vitamin concentrates may be, and frequently are, added.

TABLE IV. FORMULA FOR TUBE FEEDINGS

	GRAMS OF PROTEIN	NUMBER OF CALORIES
Egg white (4)	12	268
Egg yolks (4)		
Milk (1,000 c.c.)	30	675
Evaporated milk (210 c.c.)	17.5	311
Plain malt (⅙ lb.) ½ lb.	10.0	307
Dextrin (⅙ lb.) or	---	307
Sugar (⅙ lb.) 250 Gm.	---	301
Orange juice (or 100 c.c. tomato juice)	1.2	40
Total	70.7	2,209
Makes a total of 1,500 c.c.		
Cook first four ingredients as soft custard.		
Add orange or tomato juice after cooking; strain.		
Add vitamin concentrates if desired.		
One cubic centimeter equals approximately 1.5 calories.		

Abbott,[22] in discussing feeding mixtures for use in jejunal alimentation, has stressed the following points: (1) The normal fasting jejunal contents are hypotonic. (2) The maximal glucose concentration that normally enters the duodenum, from the stomach, is 15 per cent. (3) The maximal sugar concentration obtained from the jejunum, after glucose ingestion, is 6 per cent. (4) Hyperperistalsis is produced by the introduction into the intestines of any glucose solution, in excess of these values. (5) In general, low concentration of amino acid and fatty acids are present in the jejunum. "In a word, it seems desirable to predigest the food to avoid the risk of there being inadequate ferments for digestion, in the sick patient. . . ."[22]

It has been found desirable to use a 5 per cent casein digest, plus a 5 per cent glucose mixture in jejunal feeding, for the first three or four postoperative days, since there is a decreased secretion of digestive ferments after abdominal surgery. This should be given in amounts, not in excess of 30 to 60 c.c. every one or two hours, to avoid distention of the bowel.

*Nurtamigen, consisting of dextrimaltose, amigen, neutral fat, arrowroot starch, calcium gluconate, brewers' yeast, and minerals added to simulate the quantities present in cow's milk; manufactured by Mead Johnson and Company, Evansville, Ind.

A number of protein-containing fluids are available for parenteral use. In Table V are listed those that are in common use.

Whole blood is essential where there is both an anemia and a hypoproteinemia. Frequently, two, three, or more whole blood infusions will be necessary to correct the anemia. Whipple[6] has found that if there is both an anemia and a hypoproteinemia present in dogs, that the protein fed first replaces the protein fraction of hemoglobin. Accordingly, it is felt that in all operations in which there is considerable blood loss, this should be replaced by transfusions of whole blood.

After anemia is corrected, one of the fluids listed in Table V can be used. It is generally accepted that plasma is the best source of parenteral protein for elevation of low serum protein. It should be re-emphasized that even with plasma it is not practical to give large enough amounts to raise a markedly decreased serum protein. Strumia and co-workers[23] have calculated the need in severely hypoproteinemic patients, during the preoperative and postoperative periods, who can take little food orally, at 13 L. of plasma, or the equivalent of fifty-three donors. Its chief value is in the treatment of shock and during the first few days after operation, when it may partially meet the body protein needs.

TABLE V. PROTEIN-CONTAINING FLUIDS AVAILABLE FOR PARENTERAL USE

1. Whole blood
2. Human blood plasma (whole or lyophilized)
3. Human blood albumin
4. Ascitic fluid
5. Digests of casein or amino acid mixtures

Human albumin is of great value, especially in the presence of edema. It has been found that approximately 18 c.c. of fluid will be drawn into the blood stream for each gram of albumin given. It must be remembered, however, that it lacks fibrinogen, prothrombin, and globulin with its antibodies, and as there is a need for all of these in most patients, before and after major surgery, that shortcoming is apparent. At the present time, albumin is difficult to obtain, except in a few medical centers, and in the Army and Navy. Modified bovine albumin[24] or some of the intravenous gelatine[25] solutions, which are in the experimental stages, may eventually be the answer to meeting the body protein needs following surgery.

Ascitic fluid has been used by Davis and Getzoff[26] to improve a low serum protein, with definite evidence of elevation. It may be given either intravenously or subcutaneously, without preliminary typing or cross-matching. In the writer's experience, however, febrile reactions of a slight to moderate degree have occurred, even when the fluid was readministered to the patient source. If ascitic fluid is to be administered intravenously, only that which is crystal clear should be used.

Casein digests, or amino acid mixtures, were apparently first used in man in 1939 by Robert Elman. The most widely used amino-acid mixture is Amigen.*

*Manufactured by Mead Johnson and Company.

Amigen is a casein enzymatic digest containing approximately 85 per cent amino acids and 15 per cent polypeptides. Each gram yields 3.4 calories and 0.12 Gm. of nitrogen. The practical details involved in its preparation and use have largely been solved. Reactions are few and phlebitis is rare. A solution of 5 per cent amigen in 5 per cent glucose is apparently the most practical, and will yield 370 calories. Elman and Lischer[12] further stated, ". . . if a patient needs intravenous injections of glucose, he needs intravenous injections of amino acids even more, inasmuch as the former can be made easily from the latter, whereas there is no substitute for the nitrogeneous amino-acids."

In the writer's experience reported in this paper, confined largely to patients having cancer, who have lost weight over long periods of time, it has not been possible, or practical, to prevent a postoperative fall in serum protein by the use of parenteral feeding alone, and only after the patient began to take protein by mouth was an increase in serum protein noted.

In restoration of impaired liver function four points have proved of value: high protein, high carbohydrate, low fat diet, and lipotropic substances to mobilize liver fat.

Fortunately, in general, those things that will elevate the decreased total protein will improve the liver function. The diet mentioned previously meets these requirements, mainly, 70 per cent carbohydrates, 25 per cent protein, and 5 per cent fat.

It had been known for years that a fatty liver indicates a poor liver. The normal liver contains 6 per cent by weight of fat.[27] There is no test available for the presence of fat in the liver, but a liver containing 10 per cent by weight of fat will generally be enlarged.[27] It has been found that certain substances will replace the liver fat. Several lipotropic substances have been found to be of value in mobilizing the liver fat; among these are lecithin, cephalin, choline, egg albumin, casein, gelatin, and the amino acid methionine. Dragstedt has described a very potent lipotropic, a pancreatic hormone, which he called lipocaic.

It has been shown[28] that the administration of amino acids to patients with cirrhosis of the liver decreases the hepatic fat and increases the percentage of proteins. This is thought to be largely due to the methionine contained in the amino acids. Beattie and co-workers[29] have successfully treated a patient who accidentally took 30 to 40 c.c. of carbon tetrachloride (maximum therapeutic dose 4 c.c.) with casein digest and methionine.

In general, from the clinical standpoint, it has been most convenient to supply the lipotropic substance by means of a high protein diet. Goldschmidt and associates[30] believed that protein has the following four modes of action in protecting the liver: (1) Probably some specific, and as yet unknown, action on the liver cell; (2) replacing fat more effectively than carbohydrate, thereby making the liver less susceptible to injury; (3) through the fact that the liver is one of the chief storehouses of protein; (4) playing the major role in regeneration, which begins seventy-two hours after the original injury to the liver (in animals subject to damage with chloroform).

Choline will decrease liver lipid content and can be given parenterally as liver extract, which has a high choline content. The vitamin B complex and, better still, brewers' yeast also exert a protective action on the liver. It has been our practice to give brewers' yeast preoperatively and postoperatively in all major surgical cases, when food is being taken by mouth. There is evidence to show[31] that brewers' yeast contains some unidentified substance not found in the vitamin B complexes, which is of value in hepatic damage.

In the experiments reported here, a postoperative serum protein decrease occurred in 93 per cent of patients suffering from cancer, in spite of a preoperative high protein diet, and postoperative jejunal feedings in some cases, and the liberal use of blood and plasma. The serum protein concentration rose only after the patient had been taking an adequate diet by mouth for several days.

SUMMARY AND CONCLUSIONS

Forty-four per cent of the cancer patients studied had a preoperative total protein value below 6.5 Gm. per cent. A postoperative decline in serum protein concentration occurred in 93 per cent of the patients studied, this decline usually occurring in the first three to five days. In a small group of patients operated on for benign conditions, 83 per cent showed a fall in serum protein after operation. A postoperative decline in serum protein can be expected after most major surgical procedures.

Among the cancer patients, the postoperative decline in serum protein concentration was found to be due to albumin drop in sixteen cases, to globulin in seven cases, and to a decrease in both albumin and globulin in nineteen cases (Table II). An increase in globulin is to be expected in those patients whose postoperative course is complicated by some focus of infection. We feel that it is necessary to obtain both total and fractional serum proteins to evaluate adequately this blood constituent.

Only 30 per cent of the patients had regained their initial total serum protein concentration by the tenth postoperative day.

Evidence is presented showing that the blood loss, even at a relatively "bloody" operation such as radical mastectomy, does not entirely account for the total serum protein decline.

No correlation between the serum protein decline and liver function, as measured by the hippuric acid excretion test, was apparent in this study.

In the discussion of treatment, the difficulty of providing enough protein to prevent the postoperative serum protein decline is emphasized. It was found that, in general, serum proteins in elderly, frequently debilitated cancer patients returned to normal only after an adequate diet, by mouth, was taken for several days, only 30 per cent returning to the preoperative level within ten days after operation. The increased liver protein following the use of amino acids and methionine as suggested by Fagin and co-workers[28] should receive wider clinical investigation.

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JEJUNAL MALIGNANCY

EARL A. CONNOLLY, M.D., AND ARNOLD W. LEMPKA, M.D., OMAHA, NEB.
(From the Department of Surgery, Creighton University School of Medicine)

INTRODUCTION

REPORTS in the literature on primary carcinoma of the jejunum indicate the lesion is not only rare but also accompanied by an unfavorable prognosis. Two cases are being reported to add to the list of those with a more favorable result following surgical intervention.

REPORTED INCIDENCE

Swan,[1] in a search of the literature from 1929 to 1945, found sixty-six cases of jejunal cancer. Mayo[2] reported a series of forty cases from 1907 to 1939. Jetter[3] reported only one case over a period of nineteen years in a series of 4,308 malignancies. Boman[4] found three cases in 230,000 admissions to St. Luke's and St. Mary's Hospital, Duluth, Minn. Hunt and Kaneb,[5] reporting on 81,477 patients admitted to the Surgical Department at Worchester City Hospital from 1921 to 1928, found that out of 28,135 surgical specimens examined by the laboratory, three were carcinoma of the jejunum. Out of 2,266 autopsies, sixty-seven were carcinoma of the gastrointestinal tract but none were primary carcinoma of the jejunum. Medinger[6] reported twelve cases of carcinoma of the jejunum out of 1,456 necropsies and 41,000 surgical specimens. Mayo and Nettour[7] reported an incidence of 0.15 per cent of all carcinoma of the gastrointestinal tract to be jejunal. At Cook County Hospital, Christofferson and Jacobs[8] found 0.9 per cent of intestinal carcinoma to be cancer of the jejunum in 10,309 necropsies. A higher incidence was reported by Hunt and Kaneb.[5] They found three cases, or 2.1 per cent, out of 147 operative cases of gastrointestinal carcinoma. Brill,[9] in statistics covering 3,563 intestinal tumors, found 97.5 per cent were in the rectum, colon, and appendix. According to Homans,[10] tumors of the small intestine are very rare, more often adenocarcinoma than benign growths. The former led to a chronic sort of obstruction. Ficarra and Marshall[11] reported only twelve cases encountered at the Lahey Clinic in thirty years. According to Feldman,[12] carcinoma of the small intestine is an uncommon disease, the necropsy incidence being about 0.05 per cent. The incidence of the site of the lesion is as follows: duodenum 25 per cent, jejunum 40 per cent, and ileum 35 per cent. Harris and Rosenblum[13] and Carter[14] reported the incidence of carcinoma of the jejunum as approximately 1 per cent of all intestinal carcinomas. Nothnagel[15] reported nine instances of carcinoma of the jejunum in 3,585 carcinoma deaths or an incidence of 0.025 per cent. Bunting,[16] in 2,200 autopsies, found 104 cases of gastrointestinal cancer, four involving the small intestine and none the jejunum.

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The two cases we are now reporting are the only patients with diagnosed primary malignant tumors of the jejunum admitted to St. Joseph's Hospital since 1932. Since this time, 110,965 patients have been examined in the hospital, making an incidence of 0.0018 per cent. During this time 3,631 autopsies were performed by the personnel of the pathology department of Creighton University School of Medicine. The number of carcinomas was as follows: Esophagus, 21; stomach, 55; duodenum, 3; jejunum, 0; ileum, 0; bowel, large, 45; rectum, 20.

Some theories as to the reason for the low incidence would include those given by Brooksher,[17] who stated that there is less irritation because of the fluid content of that portion of the bowel, the alkalinity or special inhibitory action of secretions may be a factor, and the absence of any fixed or abrupt angulations all may be contributory to the decreased incidence. Heggs[18] added that the lack of stasis of the contents of the area may possibly account for the rarity of the lesion.

AGE AND SEX

Small intestine neoplasms occur during middle age. Ewing[19] reported an average age incidence of 46.5 years. Mayo and Nettour[7] found 51.0 years the age incidence for their series. The average age in Babcock's[20] cases was 46 years. However, Joyce[21] reported a jejunal carcinoma in a 25-year-old Filipino man. The literature would indicate that the lesion occurs more frequently in men than in women. Hunt and Kaneb[5] found 2:1 to be the ratio of men to women in the occurrence of jejunal carcinoma. Mayo[2] found it to be 2½ times more common in men than in women. In our two cases, one was a man, aged 40 years, and one a woman, aged 47 years.

SYMPTOMATOLOGY

Symptoms of a carcinoma of the jejunum are not stereotyped, but vary from little or no localizing symptoms to those manifested by severe intestinal obstruction.

Some patients, according to Martin,,[22] complain of vague abdominal distress, much on the order of those who are classed as neurotics. Some say they are aware of a certain mobility of the intestines and a fatigue that occurs before meals. Others experience a dizziness that cannot be explained and it is often associated with an unpredictable wave of nausea. Mayo[2] said that the two main features are recurrent attacks of intestinal obstruction with intercurrent relief and anemia associated with weakness and fatigability. The latter, he claimed, can be explained by the direct loss of blood from the ulcerated regions. Boman[4] described persistent, unexplained anemia and symptoms of intestinal obstruction as the usual findings. Weakness is found early, as is easy fatigability. Usually there is a loss of weight. In the Mayo and Nettour[7] series, there was an average weight loss of twenty-five pounds. This is probably explained by interference with normal bowel function, both in mobility and absorption. Tarry stools are seldom seen. Occult blood, however, is found if

enough stools are examined. Later, as the lumen narrows, pain may manifest itself and there may be abdominal distention with nausea and vomiting. The vomiting is usually intermittent and increases in severity as the obstruction progresses. Pain, as described by Boman,[4] varies from vague discomfort to severe colic located in the region of the umbilicus and lower quadrant of the abdomen. The time of pain interval is inconsistent but may occur one to two hours after eating. Pain in the epigastrium is a late symptom and is found after there is metastasis to retroperitoneal lymph nodes.

Vomiting progresses as obstruction increases and may be especially severe if the lesion is located in the upper portion of the jejunum. Constipation, a frequent symptom, may be alternated with a diarrhea or even normal bowel movements. Hunt and Kaneb[5] mentioned salivation as a characteristic symptom which frequently precedes vomiting. Those cases that are associated with symptoms of acute intestinal obstruction with pain, distention, and vomiting are usually found to include a polypoid carcinoma, often with intussusception. Koenig and Culver[23] reported upon two patients sent to them with diagnosis of duodenal obstruction, but their lesions, upon operation, were found lower in the gastrointestinal tract, namely, the jejunum.

PHYSICAL FINDINGS

Physical findings in cases of carcinoma of the jejunum depend largely upon the stage of the disease. Boman[4] stated that there are very few positive findings in the early stage. Later, the patient may be emaciated or cachectic and will be anemic. Distention varies but usually is present in the later stages. Horsley[24] stated that the distention may be absent, even late, if the tumor is high in the jejunum but usually quite severe if the lesion is lower. Visible peristalsis and sometimes severe peristalsis may be seen if the abdominal wall is thin. A palpable abdominal mass is usually a late finding and, if it is movable, it is highly suggestive of carcinoma of the small intestine according to Brooksher.[17]

X-RAY FINDINGS

Brooksher[17] said that x-ray diagnosis of small bowel carcinoma has been infrequent in the past and as determined by a survey of the literature the diagnosis is usually made at the time of laparotomy. X-ray findings may help in the diagnosis by demonstrating a filling defect at the site of the lesion with a compensatory widening proximal to the obstruction or, as Mayo[2] said, barium is often difficult to observe in the small intestine but its use in ruling out lesions of the stomach and large bowel will be of value.

Gabor and Hiller[25] stated that the finding of barium in the small intestine for more than eight hours warrants further effort to localize a lesion in that portion of the intestine. Although delayed emptying time of the small intestine is suggestive of carcinoma in that region, Horsley[24] added that avitaminosis, sprue, pellagra, and hypoproteinemia may also cause such a finding.

According to Feldman[12] the roentgen recognition of carcinoma of the small intestine is often difficult. A negative roentgenogram does not exclude early

cases. Its greatest value is in demonstrating an obstructive lesion. When the upper jejunum is involved, a temporary puddling of the barium is noted proximal to the stenosis. In complete obstruction, the proximal portion of the jejunum and duodenum is distended with smoothing out of Kerkring's folds.

Golden[26] said that a tumor arising in the wall and growing toward the serosa, as leiomyosarcoma sometimes does, would not be detected until it ulcerated through the mucosa or until it became large enough to encroach upon the lumen.

Detection of malignant tumors by roentgen examination depends upon the demonstration of a narrowing of the lumen with obliteration of the mucosal folds. No evidence of damage has been encountered from the administration of barium by mouth in the presence of disease of the small intestine, even with narrow constriction. In the small intestine the barium suspension remains fluid.

DIAGNOSIS

Accurate diagnosis of carinoma of the jejunum is often very difficult, but Boman[4] said that inference of small bowel malignancy may be gained from a careful history, physical examination, and the laboratory findings. However, a definite diagnosis can be made only by roentgenogram, laparotomy, or autopsy. Even in the hands of skilled roentgenologists, only 25 per cent of the lesions are demonstrable. In the Mayo[2] series of 101 small bowel cases, ony 25.7 per cent had the tentative diagnosis of small intestine lesion before operation. Although the roentgenologist is unable to demonstrate the lesion in a case presenting clinical findings suggestive of jejunal carcinoma, one is justified in doing a laparotomy in order to make a definite diagnosis. As Boman[4] further stated, a thorough abdominal search should be made as concurrent diseases such as cholecystitis, duodenal ulcer, etc. may overshadow the picture produced by jejunal carcinoma.

Primary malignant disease of the small intestine must be differentiated from narrowing due to inflammation. As a general rule, a malignant constriction is short while an inflammatory constriction is longer, being at least 8 to 10 cm. in length. Carcinoma ordinarily produces a short constriction, 2 to 4 cm. in length.

PATHOLOGY

Malignant lesions of the jejunum are usually adenocarcinoma and are similar to the type seen in the colon. Mayo[2] reported forty cases, with thirty-one being adenocarcinoma, two leiomyosarcoma, one epithelioma, and six in which there were no pathologic specimens. Boman[4] reported that 90 per cent of the carcinomas of the small intestine are of the adenomatous type, usually annular or constricting, but may be polypoid, ulcerating, and nonconstricting. Heggs[18] reported that the majority of the lesions are located in the proximal portion of the jejunum. Ewing[19] stated that tumors of the small intestine may produce polypoid outgrowths obstructing the lumen, the lesions may ulcerate early, or the main result may be stenosis from invasions of muscular or subserous coats. Often there is dilatation of the bowel above the tumor and when the tumor lies

in the upper jejunum the disease may simulate pyloric stenosis. Babcock[20] said the annular type arises from mucosal glands and, therefore, has the histology of adenocarcinoma.

PROGNOSIS

As Boman[4] said the prognosis of any small bowel carcinoma is discouraging whether the growth is removed or not. Rankin and Mayo[27] reported in 1930 that no patients lived over three years and also added that one-third of them had hopeless metastases at operation. McDougal[28] reported that resection of the small bowel is followed by 40 per cent mortality and that about 5 per cent of the patients with small bowel carcinoma have a five-year cure. Mayo[2] reported a higher incidence of five-year cure, giving 12.3 per cent as his figure for a series of sixty-six cases. Medinger[6] reported on twenty-two cases from Boston sources, of which nineteen patients were operated upon with 47 per cent mortality. Of those that lived, three were well with no recurrence for periods of eleven years, three years, and less than one year. In the Mayo and Nettour[7] report, only four out of seventy-six were alive at the time of writing, the average duration of time for those who lived was 17.6 months. Two lived seven years. Babcock[20] gave an operative mortality of 17 per cent and a recurrence of 75 per cent. Gatch[29] stated that the results of resection were almost totally bad because of the presence of early metastases. Ficarra and Marshall[11] said that the prognosis with or without treatment is discouraging; the duration of life after resection was given as one year to seventeen or eighteen months.

CASE REPORTS

Case 1 (No. 54289).—N. L., a white man, aged 40 years, entered St. Joseph's Hospital on Nov. 29, 1932, with a history of weakness, vertigo, and melena. He had been treated for peptic ulcer about five months. Physical examination revealed an exsanguinated man with some tenderness in the epigastrium. Hemoglobin was 34 per cent and red blood cells were 2,820,000. Diagnosis was made of bleeding duodenal ulcer. He was given blood transfusions, placed on an ulcer regime, and discharged three weeks later.

On Aug. 1, 1933, he re-entered the hospital with the same history, namely, weakness, vertigo, and melena. Hemoglobin was 60 per cent and red blood cells were 3,480,000. Diagnosis was again made of bleeding duodenal ulcer. He was given transfusions, placed on an ulcer regime, and discharged three weeks later. On June 8, 1938, he re-entered the hospital because of weakness, vertigo, and melena. Hemoglobin was 43 per cent and red blood cells were 2,470,000. He was again given transfusions, placed on an ulcer regime, and discharged three weeks later. He then consulted the Mayo Clinic where the diagnosis was confirmed and he was advised that if further bleeding occurred, surgery was indicated.

On Oct. 4, 1938, he re-entered the hospital because of weakness, vertigo, and melena. Hemoglobin was 37 per cent and red blood cells were 1,970,000. He was given transfusions, continued on ulcer regime, and discharged six weeks later. On Aug. 15, 1939, he re-entered the hospital because of melena. Hemoglobin was 90 per cent and red blood cells were 4,430,000. He remained in the hospital five days. On Jan. 5, 1940, he re-entered the hospital with a complaint of weakness and melena. There was a painful area over the right rectus muscle, below the umbilicus. There was a questionable mass palpable. Hemoglobin was 80 per cent and red blood cells were 4,150,000. He was treated medically and discharged two weeks later.

He was again admitted to the hospital on Feb. 5, 1941, because of weakness, vertigo, and melena. Hemoglobin was 39 per cent and red blood cells were 2,600,000. There was a palpable mass in the right abdomen. He was treated medically and discharged seven weeks later with instructions to return for an operation when his condition improved. Although, over a period of eight years, there were frequent episodes of massive hemorrhage producing weakness, dizziness, and syncope attributed to duodenal ulcer, there never was any pain, dyspepsia, nausea, or vomiting.

He re-entered the hospital on May 18, 1941 for operation. The hemoglobin at this time was 106 per cent and red blood cells were 5,260,000.

Fig. 1.—Photograph of surgical specimen removed, showing resected jejunum and large tumor projecting from antimesenteric border.

An operation was done on May 19, 1941. Under ether anesthesia, a tumor the size of a large orange was found on the antimesenteric border of the jejunum. It was resected and an end-to-end anastomosis was done. He was dismissed from the hospital on June 13, 1941.

Pathologic Report.—Gross specimen revealed a resected piece of small bowel 12 cm. long, with distended vessels on the surface and a firm smooth globular mass 6 cm. in diameter projecting from the convex surface beneath the serosa. When the bowel was opened the lumen led into part of the projecting nodule which was soft, red, and resembled muscle. The mucosa of the bowel around the opening into the tumor was thickened and edematous. The rest of the tumor nodule was a cavity filled with fluid blood and partially lined with layers of fibrin lying on a smooth lining. (See Fig. 1.)

Microscopic report on sections taken from the substance of the large tumor mass, the margins of the diverticulum from the bowel and from the wall of the large area containing the hemorrhage, revealed essentially the same picture. The tumor was made up entirely of large elongated cells, with hemorrhage here and there and many hyalinized small zones. There were scattered pyknotic nuclei and a rare cell containing several nuclei and giant in

size. Both hematopylin—eosin and Masson Trichrome stains were used. The histologic picture was one of a muscle tumor with enough growth activity to merit the designation of leiomyosarcoma of an apparently low grade of malignancy. (See Fig. 2.)

Diagnosis was encapsulated large polypoid subserous leiomyosarcoma, grade I, of the small intestine, with diverticulum and hemorrhage into tumor.

Remarks.—Such lesions tend to recur if incompletely removed, and metastasize late to lungs and liver. They are radioresistant. Isolated cases of permanent cure are recorded. This particular lesion was of a low-grade malignancy.

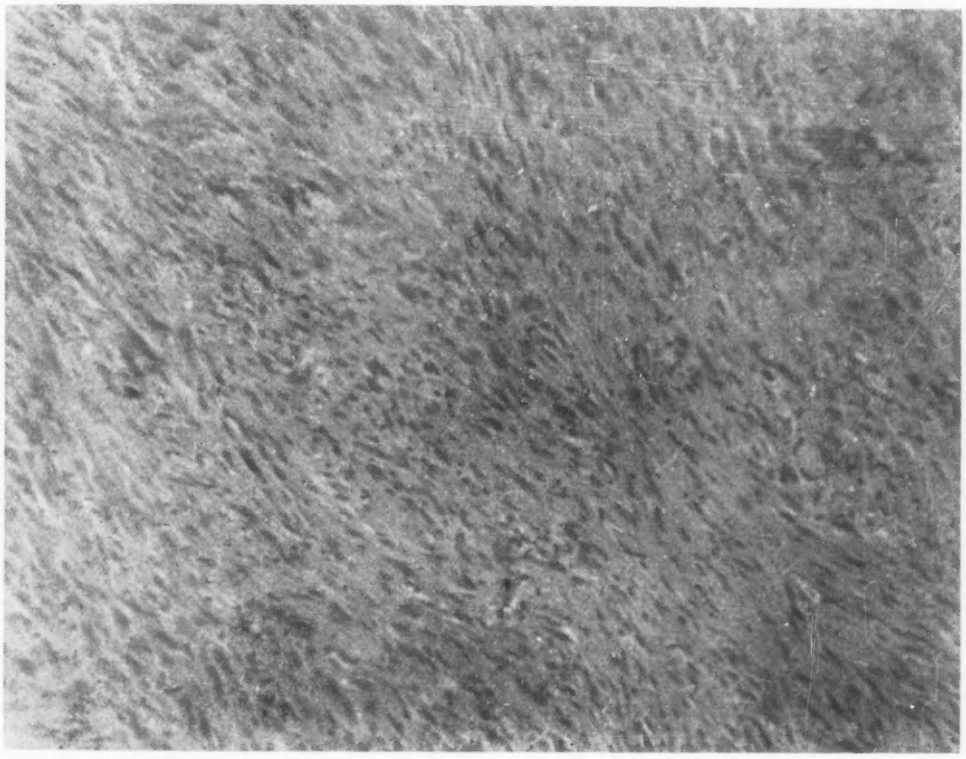

Fig. 2.—Photomicrograph of leiomyosarcoma of jejunum, showing elongated smooth muscle cells with some pleomorphism (low power).

The patient was examined on May 19, 1946, five years after resection of the tumor. Since the jejunal resection he has worked at his occupation as cabinetmaker, except for temporary absences, at which times a bladder stone was removed suprapubically, transurethral resection of a hypertrophied prostate was performed, and drainage of a perinephritic abscess was done. He is in excellent health. However, he wears an abdominal support because of an incisional hernia. This will be repaired in the near future.

CASE 2 (No. 37196).—A. K., a white woman, aged 47 years, entered St. Joseph's Hospital on Aug. 9, 1939, complaining of frequent vomiting and a paroxysmal type of pain in the abdomen. The patient had been in good health until about six months before admission. At that time she suffered severe pain in the abdomen, lasting two or three hours. This came on after gorging herself with popcorn. She did not vomit, but was very sick. Three months later she developed a suffocating feeling that seemed to start in the abdomen and gave her the feeling of "dying." Occasionally this was associated with vomiting. Five weeks before admission she suffered a severe vomiting attack that she attributed to the ingestion of gin, and this was the beginning of the severe sickness. She became progressively

worse and would vomit almost every time she ate. The feeling of suffocation became more and more severe. During the last month of the illness she developed a pain that often started in the region of the right costovertebral angle and radiated anteriorly to the region over the gall bladder. Vomiting recurred frequently, was projectile in character, and unaccompanied by nausea. The emesis was green in color and contained particles of undigested food. There was no gross blood in either vomitus or stool, the latter, too, was said to be green. There was a loss of sixteen pounds of weight during the last two months of the illness. Past history was noncontributory.

Fig. 3.—X-ray picture of abdomen taken twenty-four hours after barium meal showing dilated jejunum proximal to constriction.

Physical examination of the head and neck gave negative results. The chest was clear, heart regular, and there were no murmurs. Blood pressure was 174/110. There were no masses or areas of tenderness in the abdomen. She was moderately obese, weighing 171 pounds.

Laboratory Report.—Blood count was: hemoglobin, 107 per cent (15.4 Gm. equal 100 per cent), red blood cells, 5,370,000; white blood cells, 16,600; monocytes, 1 per cent; lymphocytes, 16 per cent; neutrophiles, 83 per cent; staffs, 4 per cent; segments, 79 per cent. Urinalysis showed specific gravity, 1.032; acid reaction, trace of albumin; sugar, negative. Myxomatous amorphous urate crystals. Wassermann and Kahn reactions were negative.

X-ray Report.—Examination of the chest was negative. Preliminary films of the gall bladder area showed no definite pathology. Esophagus was negative. The stomach filled well, action was good, negative. Pylorus and duodenum filled well, negative. In the upper portion of the jejunum there was apparently a marked degree of obstruction. Practically all of the barium was still retained proximal to this point at a seven-hour observation. Twenty-four hours later the barium had failed to pass through the obstruction previously reported in the jejunum. There was a very definite dilatation of the proximal jejunum. (See Fig. 3.)

Treatment.—Wangensteen suction was started; intravenous fluids, and morphine for pain, were administered for two days prior to operation. Operation was performed on Aug. 11, 1939. Through a left paramedian incision centering on the umbilicus, the small bowel was explored. Twelve inches from the duodenal-jejunal junction a firm annular constricting growth was found.

Fig. 4.—Photomicrograph of adenocarcinoma of small bowel invading submucosa.

Pathologic Report.—Gross specimen was a resected piece of small bowel 8 cm. long and 3 in. in diameter. Vessels were deeply engorged. The mid-portion was narrowed and within the lumen a firm mass could be felt. On opening the segment a soft gray mass filled the lumen of the central segment. It was papillary and sprang from the mucosa.

Histology revealed a papillary tumor mass in which the thin papillae were covered by one or more tall hyperchromic epithelia. There was some invasion of the submucosa by these papillae and by glands lined by similar cells.

Diagnosis was Papillary adenocarcinoma of the jejunum, grade II. (See Fig. 4.)

Remarks.—After an uneventful convalescence, the patient left the hospital on the twenty-first postoperative day.

Examination on May 19, 1946, six and one-half years after operation, showed the patient to be entirely well and working every day. Weight is 195 pounds.

SUMMARY

Two patients having had jejunal malignancy are reported who are alive and well five and six and one-half years after resection.

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AMPUTATION OF THE INDEX RAY

CAPTAIN JAMES H. MAHONEY, LIEUTENANT COLONEL GEORGE S. PHALEN,
AND COLONEL WILLIAM H. FRACKELTON, MEDICAL CORPS,
ARMY OF THE UNITED STATES

(From the Hand Section of Surgical Service, William Beaumont General Hospital, El Paso, Texas)

THE thumb is the most important digit of the hand, and the index finger ranks second only to the thumb in importance. Because the index finger is more important functionally than the other fingers, surgeons have been taught to salvage as much of this finger as possible when treating an injury to this digit.[2] In treating a large number of cases on a hand service of an Army general hospital, we have found that salvaging all or part of an injured index finger may often result in a loss of efficiency in the use of the hand. This is especially true when the index finger must be amputated at any point proximal to the proximal interphalangeal joint. In these cases an amputation of the index ray (index finger together with the second metacarpal bone) has resulted in a restoration of almost normal function in the injured hand. Because it is apparent that the general surgeon may not be too familiar with this type of operative procedure and its indications we feel justified in publishing this report.

We have recommended amputation of the index ray only in patients with normal, or nearly normal, function in the remaining digits of the hand. These cases fall into two groups: (1) Patients with the index finger amputated proximal to the proximal interphalangeal joint, and (2) patients with the index finger so badly damaged that any reconstructive surgery would hold little promise of restoring a fairly normally functioning digit.

The only absolute indication for amputation of a finger is loss of blood supply of sufficient severity to produce ischemic necrosis. Even though the blood supply of a finger may be adequate, amputation of the digit may be indicated if there has been sufficient damage to the tendons, nerves, and joints so that reconstructive surgery will not produce a well-functioning finger. A poorly functioning index finger of normal length may add its minimal function to the total effort of the hand, but while doing this, it also robs the remaining normal digits of a portion of their combined functions. Dexterity may be greatly impaired because of the strategic position which the injured index finger holds between the normal thumb and remaining normal fingers. If the index finger cannot be opposed strongly and painlessly to the thumb, the patient then automatically substitutes the normal long finger for this pinching action. We have observed that the long finger is capable of adequately assuming all the duties of an index finger.

Time and money may also be factors which must be considered in deciding whether a finger should be amputated or reconstructed. The patient may not be

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able to afford a prolonged hospitalization or the multiple operations necessary to reconstruct a damaged finger. If the surgeon feels confident that he will be able to restore a damaged index finger to a fairly normal functional state, then the reconstructive surgery indicated should certainly be done. But the patient may lose much time and money in a vain effort to salvage an index finger which is too badly damaged ever to function normally again.

Instead of spending six to eighteen months in a futile attempt to restore the index finger to normal, the patient might find it to his advantage to submit to an amputation of the index ray and return to work within twenty-eight days.

If the index finger can be amputated through the middle phalanx, the digit will still be sufficiently long to permit an adequate pinching action between the tip of the thumb and the end of the amputated finger. Furthermore, with a normal painless range of motion still present in the proximal interphalangeal joint, the index finger will be of considerable aid in the grasping of objects. If, however, the index finger must be amputated at any level proximal to the proximal interphalangeal joint, there will remain a stump which will be of very little functional value. In fact, this short index stump actually may reduce the efficiency of the hand.

Patients who have had an index finger amputated through the proximal phalanx state that the index stump hinders the otherwise normal function of their hands. They are constantly bumping the end of the stump while doing any work with their hands. In grasping an object, the index stump may even push against the object grasped. In shaking hands, the short stump may also be in the way. There is no longer any adequate pinch between the short index stump and the thumb, and the long finger is hindered to some extent in taking over the normal function of the index finger because of the interposition of the index stump between the long finger and the thumb.

The following case reports illustrate quite well the type of patient for whom an index ray amputation is indicated.

CASE REPORTS

CASE 1.—A 21-year-old master sergeant in the infantry was wounded in combat on Dec. 13, 1944, in Belgium. He sustained multiple wounds, including partial traumatic amputation of the right and left index fingers and the left thumb. The soldier was taken prisoner and the initial débridement and primary closure of the wounds were performed by a German medical officer. The wounds healed without infection, leaving the soldier with an amputation of the right and left index fingers through the proximal half of the proximal phalanx and an amputation of the left thumb through the base of the distal phalanx.

The soldier arrived in the United States on July 1, 1945. He was granted several convalescent furloughs, during which time he worked as a clerk and truck driver in an express agency. He was admitted to the hand service of this general hospital on Jan. 12, 1946. Examination of the right hand revealed normal long, ring, and little fingers; the thumbnail was deformed due to a minor injury in the region of the nail bed, but function of this digit was not impaired; the index finger was amputated through the proximal half of the proximal phalanx. The index finger stump was well covered with an adequate volar skin pad; there was point tenderness on the dorsoradial side of the stump. The end of the stump appeared somewhat bruised. Active range of motion in the second metacarpophalangeal joint was from 180 degrees extension to 90 degrees flexion. There were multiple small metallic foreign bodies

on the dorsum of the hand visible on roentgenogram, and three were palpable in the subcutaneous tissue over the third metacarpal and the proximal phalanx of the ring finger.

Examination of the left hand revealed normal long, ring, and little fingers. The thumb had been amputated through the base of the distal phalanx, and there was an inadequate pad over the end of the stump. The index finger had been amputated through the proximal half of the proximal phalanx, leaving a very short stump. The web between the index and

Fig. 1.

Fig. 2.

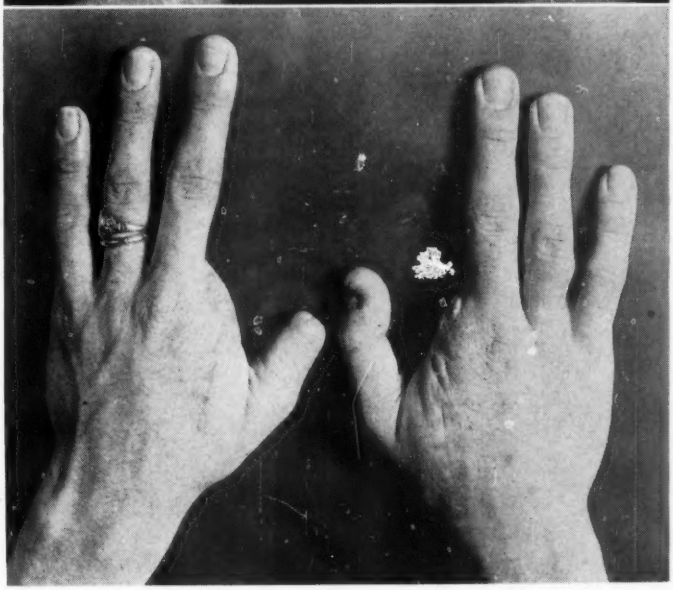


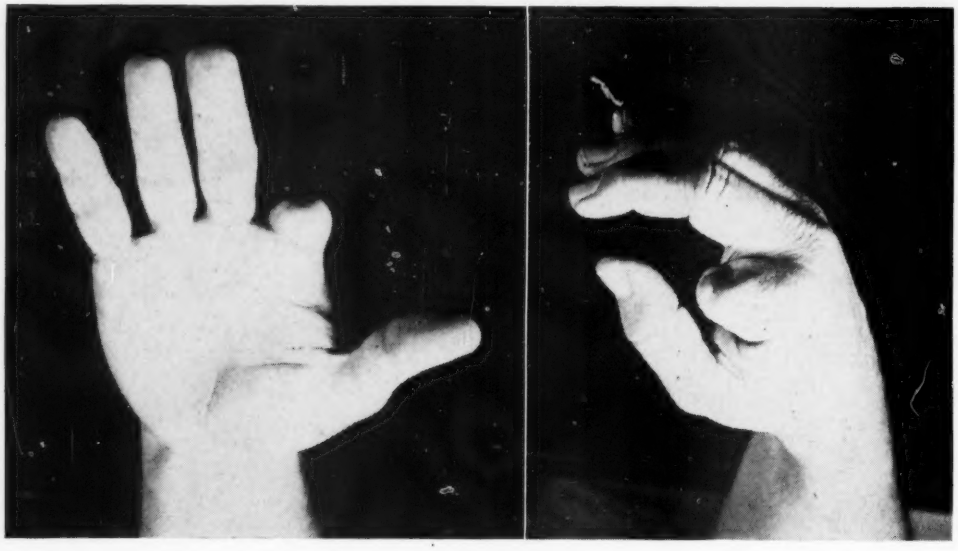
Fig. 1 (Case 1).—Dorsal view of both hands. Both index fingers have been amputated through the proximal half of the proximal phalanges, leaving very short stumps. The soldier complained that these short index stumps were constantly hindering him in the efficient performance of manual labor.

Fig. 2 (Case 1).—Dorsal view of both hands, following index ray amputations. There is no longer any obstacle between the thumb and fingers.

middle fingers had been drawn somewhat distally when the index stump was closed, but there was still active motion in the second metacarpophalangeal joint of 180 degrees extension to 90 degrees flexion. There was no point tenderness over the index stump, but the end of the stump appeared somewhat bruised.

On admission, the soldier made the following statement: "Something has to be done with these forefinger stumps, as they are always in my way. I bump them so often they get tender."

On Jan. 18, 1946, the soldier had bilateral index ray amputations with plastic revision of the amputation stump of the left thumb and removal of the three palpable metallic foreign bodies from the dorsum of the right hand. The operative incisions healed by primary intention. On the twenty-first postoperative day, active motion of the fingers and wrist was instituted. Physical therapy, consisting of whirlpool baths and massage, was given for one week to aid in the return of normal motion in the fingers of both hands. On the twenty-eighth postoperative day, the soldier was discharged from the Army on a certificate of disability. He returned to his former civilian occupation as a clerk and truck driver in an express agency, and at this time he is performing the work much more efficiently than he could prior to amputation of the index rays.



A. *B.*

Fig. 3 (Case 2).—*A*, Volar view of the right hand. The index finger has been amputated through the middle third of the proximal phalanx, leaving a short stump of very little functional value.

B, Side view of same hand, showing how the short index stump may interfere with the normal function of the remaining digits.

CASE 2.—A 26-year-old first lieutenant, serving as a paratrooper in the infantry, was wounded in combat on Oct. 2, 1944, in Germany. He sustained multiple wounds, including a partial traumatic amputation of the right index finger. The wound of the right hand was treated by débridement and primary closure.

The officer was transferred to this general hospital on July 26, 1945, primarily for further treatment of an ununited fracture of the left femur. In addition, he requested consultation with the hand service because he felt that the right hand would be more serviceable if the stump of the index finger were amputated. This index finger stump was so short that it could not be opposed to the thumb and did not aid in grasping objects. He stated, "I am constantly bruising this stump when I use my right hand. This stump seems to draw bumps."

Examination of the right hand on June 8, 1946, revealed normal thumb, long, ring, and little fingers. The index finger was amputated through the middle third of the proximal phalanx, and the end of the stump was well covered with an adequate skin pad. Active range of motion in the second metacarpophalangeal joint was from 180 degrees extension to 100 degrees flexion.

A. *B.*

Fig. 4 (Case 2).—*A*, Volar view of right hand, following index ray amputation and flexor tendon transfer at the wrist.

B, Side view of same hand, showing that the long finger now may assume the full duties of a normal index finger.

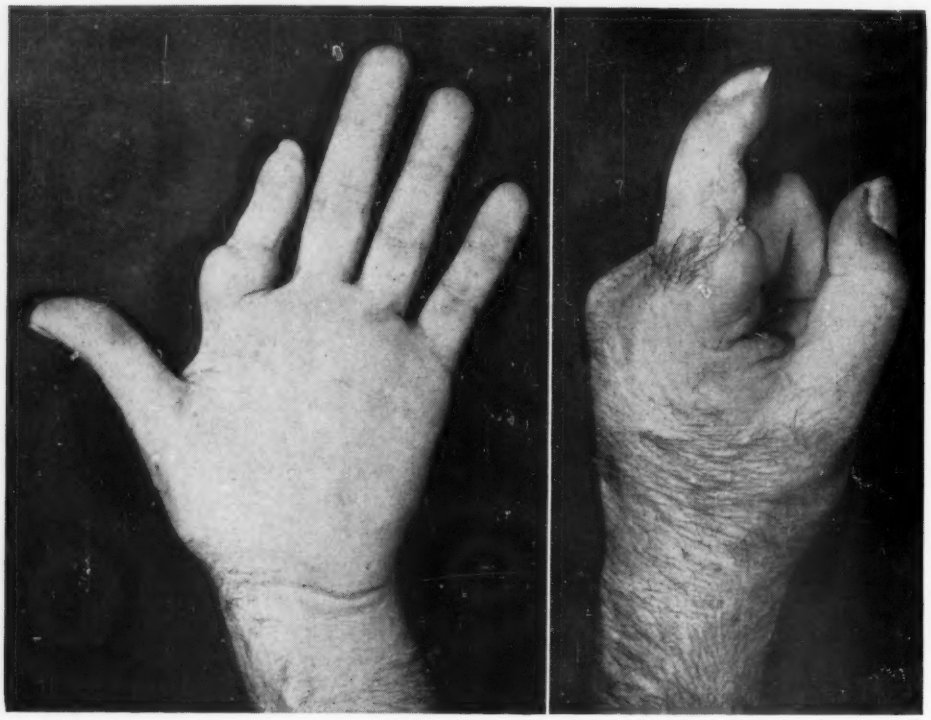
On June 10, 1946, amputation of the right index ray was performed, with a transfer of the flexor profundus tendon of the index finger into the flexor profundus tendon of the long finger at the wrist. The operative incisions healed by primary intention. Physical therapy, consisting of whirlpool baths and massage, was given for two weeks to aid in the restoration of normal motion in the fingers and thumb. The patient experienced some discomfort at the site of tendon transfer at the wrist when starting active motion in the fingers, but this subsided in a few days.

Although this patient is still hospitalized for further treatment of the fractured femur, he has already found that he is better able to use the right hand in walking on crutches or in performing other manual duties about the hospital.

CASE 3.—A 28-year-old Army sergeant was taken prisoner at Bataan. While working as a prisoner of war in a coal mine, he sustained an injury to the left hand on June 6, 1945. The left index finger was crushed by a falling stone. A Japanese medical officer sutured the jagged laceration along the proximal phalanx of the finger without any previous cleansing or débridement of the wound. The finger became infected, and osteomyelitis developed in the proximal phalanx. A curettement of the draining wound was performed in September, 1945, and the index finger was placed in traction in a banjo splint when the soldier was evacuated

to the United States. The wound healed by January, 1946, while the soldier was a patient in an Army general hospital. At that installation, the soldier requested that the index finger be amputated; but the opinion of the medical officers was that the finger should be saved. The soldier was transferred to another general hospital, where amputation of the index finger was again refused because the medical officers felt that this digit should be saved if at all possible.

The soldier was transferred to the hand service of this general hospital on May 24, 1946, for further evaluation and disposition. He still maintained that the injured finger was in his way and that the function of the hand would be improved a great deal by amputation of the index finger.



A. *B.*

Fig. 5 (Case 3).—*A*, Volar view of left hand. Although the index finger has normal sensation, its joints and tendons have been irreparably damaged.

B, Side view of same hand, showing how the damaged index finger interferes with the function of the remaining normal digits.

Examination of the left hand revealed a normal thumb, long, ring, and little fingers. The index finger was shortened three-fourths of an inch. There was a cicatrix on the radial side of the proximal phalanx, extending to the distal interphalangeal joint. Sensation was normal throughout the entire index finger. Range of motion in the second metacarpophalangeal joint was from 180 degrees extension to 110 degrees flexion; the proximal interphalangeal joint was fixed by bony ankylosis at 180 degrees; and the distal interphalangeal joint was also fixed at 150 degrees by a firm fibrous ankylosis. Roentgenograms revealed a healed comminuted fracture involving the shaft and head of the proximal phalanx and the base of the middle phalanx, with evidence of chronic osteomyelitis in the proximal phalanx and bony ankylosis of the proximal interphalangeal joint.

On June 2, 1946, amputation of the index ray was performed. The operative incision healed by primary intention. Physical therapy, consisting of whirlpool baths and massages,

was given for one week to aid in the restoration of normal motion in the fingers and thumb. The patient has expressed complete satisfaction with the increased dexterity and usefulness he now has in the left hand. He finds that the left long finger performs adequately the functions of a normal index finger.

A. *B.*

Fig. 6.—*A*, Volar view and, *B*, side view of same hand as shown in Fig. 5, after index ray amputation. The efficiency of this hand has been much improved by removal of the poorly functioning index finger and restoration of a wide smooth cleft between thumb and long finger.

DISCUSSION

During the past year, we have performed eighteen amputations of the index ray. In every case, the dexterity of the hand has been improved and the patient has expressed satisfaction with the end result. The cosmetic appearance of the hand has also been improved, but we have always considered this factor to be of only secondary importance. When recommending an index ray amputation, we have been primarily concerned in the restoration of an efficiently functioning hand; the fact that the cosmetic appearance of the hand is also improved becomes purely incidental.

In performing an index ray amputation, an incision is made about the base of the index finger and then extended longitudinally on the dorsum of the hand to the base of the second metacarpal. The second metacarpal is exposed subperiosteally and osteotomized just distal to its base. The base of this bone is not removed because it is desirable to preserve the insertion of the extensor carpi radialis longus tendon.[1] If possible, the tendon of the first dorsal interosseous muscle is isolated and inserted into the tendon of the second dorsal interosseous muscle. This tendon transfer does not materially increase the range

of abduction in the long finger, but it does increase the power of the long finger to resist pressure from the thumb. The digital nerves are carefully isolated, ligated, and buried to prevent the formation of painful neuromas. Through a small separate transverse incision at the wrist, the flexor tendons of the index finger may be withdrawn and transferred into the flexor tendons of the long finger. Obviously this tendon transfer should increase the flexion power of the long finger, but it is difficult, if not well-nigh impossible, to evaluate the clinical results of this procedure. In any event, we do not believe this flexor tendon transfer is an essential part of the operation.

It is true that amputation of the index ray does narrow the breadth of the palm, and this may not be too desirable in a patient who must perform heavy manual labor. It has been our experience, however, that the increased dexterity obtained by this operation more than compensates for the slight diminution in breadth of the palm. With an amputation through the second metacarpophalangeal joint, there would still be present a stump which would be constantly traumatized and which might interfere to some extent with an adequate pinching action between the thumb and long finger. In every case where index ray amputation was advised, the patient had had ample opportunity to use and work with the injured hand. Many of the patients had received "work furloughs" of sixty to ninety days, and some had been returned to military duty. All of the patients found, through experience, that the efficiency of their hands was markedly impaired by the injured or amputated index finger; all patients agreed that, following amputation of the index ray, the function of their hands was much improved. The majority of these patients performed manual labor for a livelihood.

SUMMARY

1. Amputation of the index ray is indicated in cases with an amputation of the index finger at any level proximal to the proximal interphalangeal joint, and in patients with an injured index finger not amenable to reconstructive surgery.

2. When only the index finger has been injured, and the remainder of the hand is normal, amputation of the index ray will restore almost normal function to the injured hand.

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SURGICAL TREATMENT OF INGROWN TOENAIL

LIEUTENANT B. G. CLARKE AND LIEUTENANT K. A. DILLINGER,
MEDICAL CORPS, U.S.N.R.

EXPERIENCE with 269 patients with ingrown toenails operated upon by Winograd's technique is summarized to augment the excellent studies already published including those of Dowd,[1] Kurtzahn,[2] Keyes,[3] and Winograd,[4, 5] who presented statistical data on postoperative follow-up in their reports. The judgment of the surgeon will dictate the use of conservative treatment or selection of one of several types of operations. Each has been used successfully by its exponents in the past and present.

HISTORICAL

Michaelis[6] reviewed work done before 1830, Emmert[7] abstracted contributions from that date until 1869, and Bartlett,[8] Keyes,[3] and Wilson[9] discussed more recent reports. A description of the anatomy of the toenail may be found in *A Textbook of Histology* by Maximow and Bloom.[10]

As early as 1830, Michaelis[6] pointed out the importance of cutting the toenails square with their corners exposed and of wearing well-fitted shoes to prevent ingrown toenail. This observation has been generally agreed upon since.

Among conservative methods of treatment, Heister[6] in 1763 elevated the corner of the ingrowing nail with a sound and maintained it in position with a piece of cotton thrust under the nail corner as a splint. The same method was described by Foote,[11] Deavor,[12] Graham,[13] Dodd,[14] Kendall,[15] Winograd,[4] O'Donoghue,[16] Christopher,[17] and others. The ingrowing nail corner may also be separated from the inflamed soft tissue with inelastic materials such as metal splints described as early as 1825 by Duden,[6] lately by Foote and Livingston,[18] Klages,[19] Marton,[20] and Linch.[21] Celluloid-soaked gauze was used by Mickel.[22]

Dodd[14] gave instructions for another conservative technique which he has used successfully: the center of the nail is shaved with knife, glass, or emery board and a V-shaped notch is clipped in its end. This method, employed by LaFaye[6] in 1739, has met with the approval of many since.

Albucasim[6] treated ingrown nail in the eleventh century by excision and cautery of the exuberant granulation tissue. During the nineteenth, caustics and escharotics were widely used. Among contemporaries, Vernon[23] has successfully employed electrosurgery for the same purpose although his report does not specify the average time required for healing.

Surgical excision of the granulating soft tissue was practiced by Ambroïse Paré[6] four hundred years ago. Emmert[7] and Cotting[24] devised operations for more extensive excision of the granulating tissue together with a segment of nor-

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mal tissue from the side of the toe. As the defect healed by cicatrization the soft tissues and skin were withdrawn from the nail corner. Healing by this method, according to Cotting,[24] required four weeks. Ney[25] in 1923 described the extensive resection of soft tissue from the side of the toe followed by plastic skin closure of the defect, which required from two to three weeks for complete healing.

Retraction of the irritated soft parts from the margin of the nail is the basis also of an operation described in 1893 by Howard,[26] who excised an elliptical, wedge-shaped segment of skin and soft tissue from the uninfected area at the end of the toe and sutured the defect to withdraw the inflamed part from the ingrowing nail edge. Bartlett[8] successfully employed a less extensive incision, removing a wedge of tissue from the side of the toe to achieve the same result. These techniques require incision only through uninfected areas and favor primary healing and short convalescence.

Inflamed tissue is removed from the nail in the foregoing types of operation. In currently more widely practiced techniques the ingrowing nail margin is removed. Fabricius,[6] seventeenth century Italian anatomist and surgeon, the pupil of Fallopius and teacher of Harvey, excised and avulsed the ingrowing margin of the toenail. He was followed by Heister and Michaelis.[6] Agard,[27] Anger,[28] and Dowd[1] modified this maneuver to include excision not only of the ingrowing nail margin but of the lateral skin fold, the granulating soft tissue, and the nail-bearing matrix as well. In ten of Dowd's twenty-three cases, healing was by first intention. In 1899 Foote[11] published a less radical variation of this technique which has been discussed by Fabry,[29] O'Donoghue,[16] Christopher,[17] and others. This is called the standard or von Bergmann operation by Keyes.[30] A wedge of tissue is excised down to the periosteum of the terminal phalanx to include a strip of nail about one-fourth inch (0.5 cm.) wide, the underlying nail bed and matrix, and the adjacent lateral skin fold and ulcer. The matrix is curetted and each end of the wound may be approximated by stitches. Kurtzahn[2] reported no recurrence in twenty-five patients observed for one and one-half years postoperatively. In sixty cases studied by Keyes[3] in which the same technique was used by a group of surgeons, there were three recurrences. Sixteen days were the average required for healing in this series; in three patients healing was by first intention. In a basically similar procedure, Thurlow[31] and Bennett[32] developed methods of plastic closure which are described in their articles. Although Bennett does not give figures on recurrence, his patients were walking in three days and ready for military duty in seven.

The most radical procedure for cure of ingrowing nail is removal of the entire nail. It is generally agreed that without curettage of the matrix, recurrence is frequent. Dupuytren[6] in 1826, however, excised and avulsed the nail and destroyed the matrix. Deavor[12] and Scougall[33] described the same technique although their report does not contain statistics; among Keyes'[3] group, three patients were operated upon in this fashion with no recurrences and an average healing time of twenty-three days. Removal of nail and matrix with plastic closure of the defect by mobilization of skin flaps proximal and distal to the

site of the nail has been done by Dolan,[34] Kendall,[15] Eichelbaum,[35] Nuttall,[36] and Wilson,[9] who described their methods. In Keyes'[3] series, four cases were done by a plastic method, with one recurrence.

Winograd's technique, outlined in his articles[4, 5] and in Christopher's *Minor Surgery*,[17] is a refinement of Fabricius' made possible by use of an anesthetic. The nail-forming matrix is exposed by a small incision in the eponychium, and after removal of a one-eighth to one-quarter inch (0.3-0.6 cm.) strip of ingrowing nail, the matrix and nail bed are curetted leaving the soft tissues otherwise intact. Winograd[5] did a follow-up study on twenty cases for eighteen months, in which there were three recurrences. In Keyes'[3] series of thirty-four cases, there were four recurrences. Among twenty-nine of our Naval cases followed closely, nine recurrences were noted, two with symptoms. Among a group of 240 Marines operated upon, among whom systematic follow-up was not made, only one recurrence was known. Primary healing occurred in our entire series of 269 cases which may be attributable to favorable age group of patients, the simplicity of the procedure, and uniform preoperative preparation consisting of surgical scrub of foot with hand brush, soap, and water. Foote[11] in 1899 emphasized the importance of scrubbing and disinfecting the toe. Graham[13] used a technique similar to that of Winograd, dissecting rather than curetting the matrix. He did not give figures on recurrence.

REPORT OF CASES

Two groups of cases are included in this study. Twenty-nine operations were performed aboard a Naval vessel. These represented an annual incidence of 29 per 1,000 men. Two hundred forty operations were performed upon men of an expeditionary unit of Marine infantry, representing an annual incidence of 113 per 1,000 men. Each operator used Winograd's technique without modification, using digital nerve block with procaine hydrochloride.

Conditions aboard ship favored preservation of records and extended follow-up. The twenty-nine operations were done on twenty sailors whose average age was 25 years, between 18 and 30. No case was included in the study on which follow-up was for less than three months, which proved to be enough time to detect recurrence. The average period of observation was eight months, the longest, eighteen. The operation was performed only when pain was caused by an ingrown toenail, with or without marked soft tissue hypertrophy and granulation. In five men paronychia and abscess formation had occurred previously. Two men had operations elsewhere for ingrown toenail with recurrence. In all cases, the great toe was affected, in six the right only, in seven the left only, in seven, both big toes. Twenty-one operations were on the medial nail margin, four on the lateral margin, and two on both sides of the toe, making twenty-nine operations in all. When infection was present, several days' treatment were directed toward its amelioration or localization by conservative methods.

In each of these cases the patient scrubbed his foot before operation using a surgeon's hand brush, soap, and water in the fashion of a surgeon's hand scrub for ten minutes, under the supervision of the surgical corpsman. Skin was

prepared with tincture of merthiolate, 1:1000, and aseptic technique was employed. In every case primary healing occurred without infection. Postoperative discomfort was negligible; mild sedatives or analgesics were used occasionally. Petrolatum gauze and a snug bulky dressing were applied at operation and left for six to twenty-four hours during which the man remained in his bunk with the foot elevated. He was then allowed up with dry sterile dressing which became unnecessary after the fourth to seventh day. Men returned to duty, depending upon the nature of their work, in two to five days. In nine cases, or 31 per cent of the group, small regrowths of nail appeared from the curetted nail bed, two of which eventually caused pain.

Among the Marines, follow-up was more difficult. It was the surgeon's impression that the relatively high incidence of the disorder in this group of infantrymen was accounted for by heavy shoes and tropical expeditionary conditions. When necessary, conservative preoperative treatment was administered to reduce infection in the involved toe. Each patient was required to scrub his foot for five minutes with hand brush, soap, and water before operation under supervision of a hospital corpsman. Skin was prepared with tincture of merthiolate, 1:1000, and modified sterile technique, without gloves, was observed. Winograd's operation was performed, in a few cases modified to the extent that when large mass of exuberant granulation was present this was excised. Sterile crystalline sulfanilamide and petrolatum gauze were applied. The patient remained on a cot for twenty-four hours with the foot elevated, when the dressing was replaced by dry sterile gauze and he was allowed up. Healing was by first intention in all cases. Men were ready for full military duty, without dressings, in three to five days. Because of high casualty rates and combat conditions, accurate records and follow-ups were not kept. In only one instance, however, did a case of recurrence come to the surgeon's attention.

COMMENT

Survey of existing publications indicates that prevention of ingrown toenail depends on trimming the ends of the toenails square and the use of well-fitted shoes. Acceptable methods of conservative treatment include elevation of the ingrowing nail corner and splinting with cotton or other material; or shaving the center of the nail and notching its free end. Electrosurgery as well as several techniques for excision of exuberant granulation tissue have been employed, although healing may require some time in certain of these techniques. The nail and its matrix may be removed completely and allowed to heal by granulation, or the defect may be closed by mobilization of skin flaps and plastic repair. Another technique is the removal of a wedge-shaped block of tissue including the ingrown strip of nail, adjacent skin fold, and granulation tissue, with curettage of the nail matrix and bed. Of eighty-three patients treated thus, cases in which figures are available, three had recurrences. Winograd's technique consists of removal of a nail strip including the ingrowing part and curettage of the nail-forming matrix and nail bed through a small eponychial incision leaving the soft tissues otherwise intact.

Among the cases in which follow-up was carried out by Winograd[5] and Keyes,[3] seven of fifty-four included recurrences. In the present study, primary healing occurred in all of 269 cases, which may be attributable to favorable age of the patients, the simplicity of the procedure, the use of aseptic technique, and uniform preoperative preparation of the foot by surgical scrub with hand brush, soap, and water. Among closely followed Navy personnel there were nine recurrences in twenty-nine cases, two with symptoms. Among 240 Marine infantrymen who were not followed, only one recurrence came to the surgeon's attention.

SUMMARY

1. Results of operation for ingrown toenail by Winograd's technique in 269 cases are considered, and other conservative and operative methods of treatment are discussed.

2. Primary healing occurred without infection in all cases, which may be attributable to favorable age of patients, simplicity of procedure, use of aseptic technique, and uniform preoperative preparation of the foot by surgical scrub with hand brush, soap, and water.

3. In twenty-nine closely followed cases, there were nine recurrences, two with symptoms.

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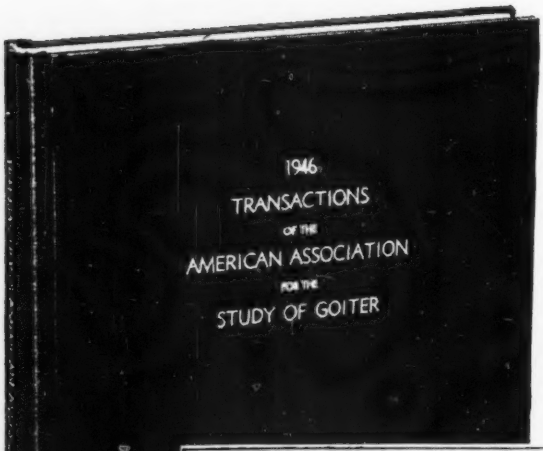

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